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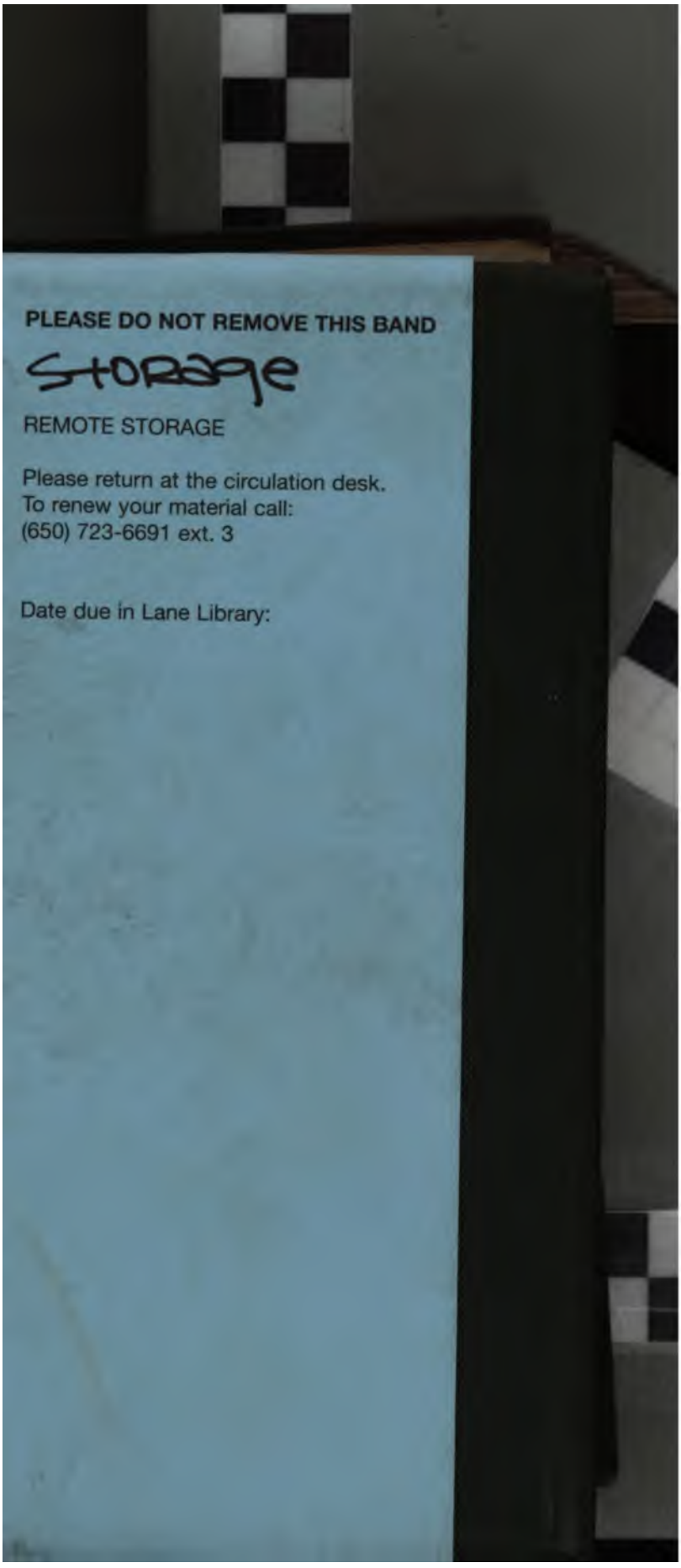
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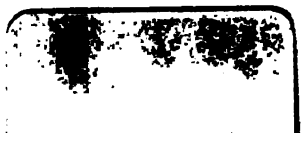


SYPHILOLOGY AND VENEREAL DISEASE

PLATE I.

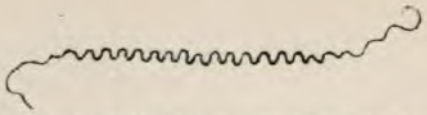


FIG. 1.—SPIROCHÆTA PALLIDA, SHOWING FLAGELLA AT EACH END. × 4,000. (AFTER SCHAUDINN.)

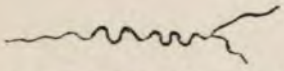
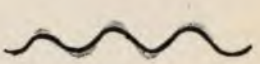


FIG. 2.—SPIROCHÆTA PALLIDA WITH TWO FLAGELLA AT ONE END. (AFTER SCHAUDINN.)



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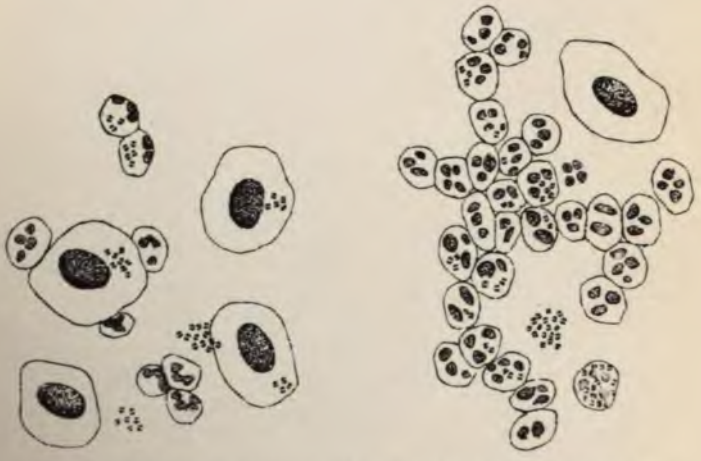

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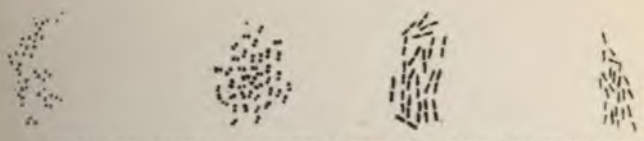

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Frontispiece

SYPHILOLOGY

AND

VENEREAL DISEASE

BY

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SECOND EDITION

NEW YORK
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PREFACE TO SECOND EDITION

SINCE the first edition of this book was published much work has been done in syphilology and venereology, and the time seems ripe to take stock of the recent additions to our knowledge. These include the method of serum diagnosis of syphilis introduced by Wassermann, Neisser and Bruck; attempts to obtain a cutaneous reaction in syphilis and gonorrhœa; the treatment of syphilis with organic preparations of arsenic, culminating in the much debated '606'; further researches in microbiology and experimental syphilology; and the vaccine treatment of gonorrhœa. I have given an account of these subjects in Chapters XXVII. to XXX.

My thanks are due to Professor Gaucher and Dr. Levaditi for giving me useful information, and to Dr. J. D. Rolleston and Mr. J. E. R. McDonagh for kindly revising the proofs.

C. F. MARSHALL.

NEW CAVENDISH STREET, W.
APRIL, 1912.

89005

PREFACE TO FIRST EDITION

SINCE the work on Syphilis and Local Contagious Disorders, written by Berkeley Hill and Arthur Cooper about twenty five years ago, there has been no book published in England dealing in a systematic manner with syphilis and venereal diseases. The present book may therefore be said to justify its existence, and in spite of any shortcomings, it has at any rate the merit of being up to date.

Much light has been thrown recently on the pathology of syphilis by the experimental inoculation of monkeys by Metchnikoff and Roux, Neisser, Finger, and others, and by the discovery of the *Spirochæta pallida* by Schaudinn and Hoffmann, and an account of this work will be found in the following pages. The important subject of parasyphilis, the conception of which originated with Fournier; the more recent evidence on the transmission of syphilis to the third generation; the question of paternal heredity; the syphilitic origin of general paralysis; the etiological factor of syphilis in arterio-sclerosis, aneurism, Bright's disease, cirrhosis of the liver, epilepsy, and other disorders of the nervous system, and other problems in syphilology, are discussed in this book.

The part dealing with syphilis is based chiefly on the teaching of Fournier and his disciples; that dealing with gonorrhœa on the works of Finger, Neisser, Jadassohn, and Balzer. My thanks are due to Professor Fournier for permission to quote largely from his works; to Professor Finger, the late Dr. Barthélemy, and the late Dr. Schaudinn for supplying me with useful information; to Dr. Roux, Dr. Levaditi, Dr. Luys, and Professor Finger for permission to reproduce

the illustrations; and to Dr. J. D. Rolleston for revising and criticizing the proofs.

On controversial points I have ventured to give my own opinions. I have also endeavoured to emphasize the importance of syphilis and gonorrhœa as etiological factors in disease. When we consider that they are probably the oldest diseases which afflicted mankind; that they are both extremely contagious; that syphilis is *par excellence* the hereditary disease, and may be transmitted to the third generation; that gonorrhœa is the cause of a large proportion of diseases of women, it appears difficult to overestimate their importance.

If I seem to have exaggerated their influence, I can only repeat the words of Ricord, 'On m'a fait le reproche d'avoir vu partout la vérole; moi, je repens au contraire de ne pas l'avoir assez souvent reconnue.'

C. F. M.

LONDON,
October, 1906.

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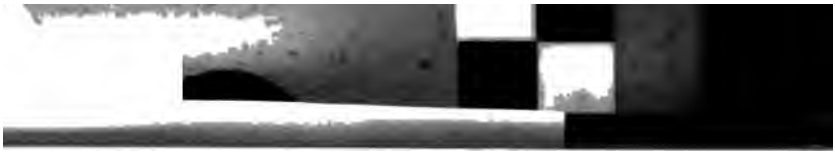

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SYPHILOLOGY AND VENEREAL DISEASE

CHAPTER I

HISTORICAL

The antiquity of syphilis has been the subject of much controversy, some authorities holding that it appeared in the fifteenth century, and was introduced into Europe by Christopher Columbus from America, others tracing it to prehistoric times.

It appears to be well established that there was a great epidemic of a new disease in Europe about the end of the fifteenth century, and that this epidemic was largely contributed to by the soldiers engaged in the invasion of Naples by Charles VIII. of France in 1494-1495; but there is evidence to show that syphilis was known in Europe before the return of Christopher Columbus, and it is much more likely that it was conveyed by his sailors in the opposite direction—from Europe to America, in the same way that Captain Cook's sailors probably introduced it into the Sandwich Islands. Fulgosi described a new disease occurring as an epidemic in 1492, three years before the return of Columbus in 1495. Although this disease was in all probability syphilis, it is necessary to note that Ricord regarded it as farcy and Cazenave as typhus.

The idea that syphilis did not exist in Europe before the end of the fifteenth century is largely due to the writings of

Astruc, who stated that there was no mention of the disease by Hippocrates and the other Greek and Latin writers. However, Lancereaux, who has investigated the origin of syphilis in a most careful manner, points out that this statement of Astruc's is incorrect. Hippocrates describes ulcers of the mouth and genital organs, ophthalmia, and swelling of the groins. Celsus mentions dry and purulent ulcers of the glans penis (*ulcera pura siccaque et ulcera humida et purulenta*). This apparently refers to hard and soft chancres. Celsus also describes the phagedenic chancre, ulcers of the mouth, nose, and tonsils, also several forms of eruption which were probably syphilitic.

According to Lancereaux, the *ficus* of the Romans and the *sykos* of the Greeks probably signified the mucous tubercle. Tertiary syphilis appears also to have been known, for Plutarch mentions erosions of the tibia, and Marcellus Empiricus describes serpiginous ulceration (*ulcera tibiarum quæ intrinsicus serpunt*).

It thus appears that soft and hard chancres and tertiary syphilitic lesions were known to the Greek and Roman physicians. Syphilis also seems to have been known to the satirical poets, for Martial writes of contagious lesions communicated to a young slave by Nævolus.

Thucydides mentions disease of the sexual organs, hands, and feet as occurring in the plague of Athens, and this plague, in the opinion of Buret, was an epidemic of syphilis.

Syphilis appears to have been known among the Hindus (1000 B.C.). According to Buret, mention is made of gonorrhœa, cystitis, orchitis, chancres, ophthalmia, papules on the face and throat, alopecia and ulcerations of the feet and hands, in the 'Ayurvedas' of Suçruta, which was translated into Latin by Hessler (*Medicinæ systema a venerabili Dhanvantari demonstratum, a Suçruta discipulo compositum*). Klein also states that mercury was used by the Hindus for the treatment of syphilis (*De morbi venerei curatione in India orientali usitata*, 1795).

The evidence of syphilis among the *Hebrews* in Biblical times is scanty and uncertain. Buret and other authors quote certain passages of the Bible as evidence of syphilis (Num.

xxv. 8 and xxxi. 16 and 17; Lev. xiii.). Hominic regards the plague of Baal-Peor as an epidemic of syphilis. In Lev. xiii. an account is given of leprosy, but whether this was true lepra or syphilis it is impossible to determine. It is known that in former times the two diseases were confounded, for syphilitic bones have been found in leprosy cemeteries by Lancereaux, Broca, and others. Zambaco has also found bones with apparently syphilitic lesions in the ancient necropolis at Cairo, showing that syphilis probably occurred among the Egyptians.

According to Dabry, the oldest evidence of syphilis is found among the Chinese. In 2367 B.C. the Emperor Hoang-ti collected the medical writings which were then existing, and these have been translated by Dabry, who states that the Chinese were acquainted with syphilis, and treated it with mercurial inunction; that they differentiated between syphilis and gonorrhœa, and that they recognised the hereditary transmission of syphilis. More recently, however, Dabry's conclusions have been questioned by a Japanese writer, Okamura, who states that, according to most of the old Japanese and Chinese authors, syphilis did not appear in China and Japan till the middle of the sixteenth century. Okamura has failed to discover the descriptions given by Dabry in the work of Hoang-ti, and found only a single reference to ulcers of the genital organs.

Scheube, on the authority of a translation of an old Japanese work in the year 800 A.D., describing affections of the genital organs, is of opinion that syphilis was known in old Japan. Okamura, however, does not accept this, so that the antiquity of syphilis in China and Japan must be considered as still unsettled.

The existence of syphilis in prehistoric times has been assumed by the discovery of human bones showing signs of syphilitic lesions. At Solutré, where prehistoric human remains have been found, a woman's skeleton was found with nodes on the tibia which were regarded as syphilitic by Virchow and Parrot. In America bones which were apparently syphilitic have been discovered by Jones and others in the Indian

graves. It is necessary to state, however, that both the syphilitic nature of the lesions and the prehistoric origin of the same have been doubted by Hyde.

The problem of the antiquity of syphilis cannot, therefore, be definitely settled, but the most reasonable view of the question seems to be that of Lancereaux, viz.: (1) That syphilitic affections seem to have been described in the most remote times, but that the connection between the various phenomena was not fully known till the end of the fifteenth century; (2) that syphilis may become epidemic under certain conditions, and is not of the same intensity all over the globe; (3) that the epidemic of 1495 developed at a time when fatigue, want of cleanliness, debauchery, and the mixing of races, combined to aggravate what was already present.

Considering that syphilis and gonorrhœa are usually contracted by sexual intercourse, it seems rational to regard them as the oldest diseases which afflicted mankind. The reason why they were better described at the end of the fifteenth century is no doubt due to the fact that this was a period of great intellectual activity.

In the first half of the sixteenth century syphilis was well described by Jean de Vigo, Jacques de Béthencourt, Ulrich de Hutten, Torella, Fernel, and others, and in 1530 Fracastor (*Hieronymo Fracastorio*), the Italian poet, philosopher, and physician, wrote his celebrated poem 'Syphilidis sive morbi Gallici,' from which the name of syphilis originated. Both Vigo and Béthencourt attributed the origin of the disease to the invasion of Naples in 1494-1495, but Fracastor believed that syphilis existed in ancient times, that its name and description were lost during the centuries, and that the same circumstances which gave rise to it formerly were reproduced in his time and caused the disease to appear again.

With regard to the etymology of the word *syphilis* opinions differ, but the most probable explanation given is that it is derived from the two words συν (with) and φιλια (love), signifying the companion of love. Previous to the appearance of Fracastor's poems the disease was known under various names, the chief of which were 'mal français,' 'mal napolitain,' and

'morbus Gallicus.' Later on it was called 'la grosse vérole,' or 'great pox,' and also 'lues venerea.'

Both Jean de Vigo and Jacques de Béthencourt advocated mercurial treatment for syphilis, but after this time mercury appears to have been superseded by guaiacum. In 1786 John Hunter wrote his 'Treatise on the Venereal Disease,' and reintroduced mercurial treatment. Hunter's work on venereal diseases was among his later writings, and cannot be regarded as his best work, for he doubted the hereditary transmission of syphilis, and upheld the identity of gonorrhœa and syphilis on the strength of the famous experiment in which he inoculated himself with gonorrhœal pus and developed syphilis (1767). This result was no doubt due to the subject from whom the pus was obtained being infected with syphilis at the same time.

In 1792 Benjamin Bell disproved the identity of gonorrhœa and syphilis by inoculation experiments on medical students who volunteered for the purpose. But it was not till more than forty years after Hunter's time that the 'unicist doctrine,' as it was called, was finally demolished by Ricord (1831-1838), who established the duality of syphilis and gonorrhœa by a series of numerous inoculations, and thus created a new era in the study of venereal diseases. The individuality of gonorrhœa was finally established by Neisser's discovery of the *gonococcus* in 1879. Ricord for a long time taught that secondary syphilitic lesions were non-contagious, and did not distinguish between simple and syphilitic chancre; but it is necessary to state that Ricord modified some of his earlier conclusions in his later years, and recognised the contagion of secondary lesions in 1859. The contagiousness of secondary lesions was established by Wallace, of Dublin, in 1835, by the inoculation of healthy subjects.

In 1850 Waller of Prague proved that the blood of syphilitics was contagious by inoculating a healthy boy with the blood of a syphilitic woman. This fact was confirmed by Pellizarri in 1860. In 1852 Bassereau established the distinction between simple and syphilitic chancres by the method of confrontation—*i.e.*, by examining both the infected and the

infecting parties whenever possible. Rollet explained the apparent exceptions to this rule by demonstrating the existence of 'mixed chancre,' due to double infection. The duality of the two kinds of chancre was subsequently confirmed by the discovery of the bacillus of soft chancre by Ducrey in 1889, and the *Spirochæta pallida* in syphilitic lesions in 1905.

There were thus two 'unicist doctrines,' both of which were proved to be erroneous; the first confounded syphilis and gonorrhœa, the second simple and syphilitic chancres.

In the middle of the nineteenth century the subject of hereditary syphilis was investigated by Diday and Ricord in France, and by Hutchinson in England; but the hereditary transmission of syphilis was recognised long before this—by Phillipus von Hohenheim (Paracelsus) in 1526, and also by Sanchez in 1785, who wrote: 'The generation procreated by these unfortunates is infected by heredity.' In 1837 Colles of Dublin announced the fact that the mother of a syphilitic infant was immune against infection. This has since been known as 'Colles' law,' but the French writers attribute the discovery of this fact to Baumes.

Syphilis of the nervous system, which was mentioned by Van Swieten as long ago as 1772, but not recognised by Hunter, was studied in the second half of the nineteenth century by Broadbent, Buzzard, Wilks, Hughlings Jackson, and Gowers in England, and by Charcot and Fournier in France. In 1875 Welsh drew attention to the syphilitic origin of aneurism, a fact which had previously been demonstrated by Morgagni in the eighteenth and by Fernel in the sixteenth century.

In 1836 Wallace of Dublin, and afterwards Ricord, introduced iodide of potassium in the treatment of syphilis; but, according to Lane, this drug was first used by Robert Williams in 1831.

Such is a brief epitome of the history of syphilis and venereal diseases, but the establishment of modern syphilology on a scientific basis is chiefly due to the work of Alfred Fournier and Rudolf Virchow. Fournier, the most distinguished pupil of the celebrated Ricord, has described syphilis from the clinical

point of view in a more complete and masterly manner than any other author, and Virchow has supplemented this by his work on the pathology of syphilitic lesions. It was Fournier who first drew attention to the syphilitic origin of tabes and general paralysis, and it is he who has extended the domain of syphilis by drawing attention to the phenomena of para-syphilis.

Finally, the pathogenic microbe of syphilis, which had so long eluded the search of many careful observers, appears to have been at last discovered by Schaudinn and Hoffmann in 1905 in the *Spirochæta pallida*. Although this organism has not at present been cultivated, and cannot, therefore, fulfil the postulates of Koch to prove its pathogenic nature, it has been found sufficiently frequently in syphilitic lesions to justify the assumption that it is the specific microbe of syphilis, and for the present may be accepted as such.

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CHAPTER II

GENERALITIES

Syphilis is a contagious disease, chronic in evolution, intermittent in manifestations, and indefinite in duration, caused by a specific microbe—probably the *Spirochæta pallida*, recently discovered by Schaudinn.

In the course of the disease inflammatory and neoplastic lesions are produced which may affect every organ and tissue of the economy. The disease may be propagated by inoculation with the blood and morbid secretions, and may be transmitted to the offspring.

The course of syphilis was divided by Ricord into three periods—primary, secondary, and tertiary—and, although it was shown by Virchow that the pathological process is essentially the same in all stages, this division into primary, secondary, and tertiary syphilis is convenient for clinical and descriptive purposes. The primary stage consists in the development of the primary sore or chancre at the point of inoculation, followed shortly afterwards by enlargement of the corresponding lymphatic glands (sympathetic bubo). The chancre is preceded by the *first incubation period*, which averages three or four weeks from the date of inoculation. Experimental inoculation, both in the human subject and in monkeys, has shown that the average incubation period of syphilis is twenty-five days.

After a *second incubation period*, averaging from forty to fifty days, the secondary period commences, during which phenomena of general infection are manifested. The duration of the secondary period is generally reckoned at two or three years, but it may be much longer, and there is no definite line of

demarcation between the secondary and tertiary periods. After the secondary phenomena have subsided, a *latent period* occurs, during which the virus is inactive, but liable to manifest renewed activity at indefinite periods. We will now consider these periods more in detail.

The Primary Period.—The chancre always develops at the point of inoculation, which is usually on the genital organs, but may occur on any part of the body which has been exposed to contagion. It is usually single, but may be multiple if several points have been inoculated simultaneously. The mature chancre is not auto-inoculable, but the experiments of Pontoppidan and Queyrat have shown that successive chancres may be reproduced by auto-inoculation up to the tenth or eleventh day. This fact shows that immunity of the organism to further infection is not established till some days after the appearance of the chancre. The chancre must nevertheless be regarded as the earliest sign of generalized syphilitic infection, for it has been repeatedly shown that excision of the chancre in its earliest stages, and even of the point of inoculation before the chancre has appeared, fails to avert secondary syphilis. Hence the failure of the attempts at abortive treatment of syphilis by excision of the chancre.

The chancre is contagious, and the *Spirochæta pallida* may be found in scrapings from the surface, or in sections. The description of the different forms of chancre and their diagnosis is given in Chapter IV.

Can syphilis develop without a chancre? Although a chancre is found in the enormous majority of cases of syphilitic infection, there are some cases in which syphilis has developed without any chancre having been found even after careful examination, and to these cases the name of *syphilis d'emblée* has been given by French authors. The majority of cases in which a chancre has been apparently absent are explained by the primary sore being an insignificant erosion which has healed up spontaneously without attracting notice; by the occurrence of intra-urethral, and possibly intra-uterine chancres, and by cases of extragenital chancre which have not been diagnosed as such. Two cases, however, have been reported

by Jullien which appear to be genuine. Two surgeons accidentally inoculated themselves while operating on a syphilitic patient; they both developed secondary syphilis, thirty and thirty-three days respectively after the inoculation; in one case there was no reaction at the site of the wound (with a needle), and in the other case there was ulceration, but in neither case did a chancre develop. In these cases the syphilitic virus was introduced directly into the blood, and the primary incubation period and chancre were absent.

Adami, writing on this point, remarks that 'it is not even necessary to have any first stage or cutaneous chancre. We know well that in every case of infection the infectious agent must enter from without into the tissues, and in a great number of cases we can discover the point or points of entry, and at such point or points we find evidence of primary local infection, whether on the skin or mucous membranes, and this local infection is strictly comparable with the cutaneous syphilitic chancre. But we also come across cases in which there is complete lack of evidence of such superficial primary infection; we may find, for instance, the cervical or mesenteric glands affected with tuberculosis without a sign of tuberculosis of the phayrnx or tonsils or intestinal mucosa. What occurs in other diseases must at times occur in syphilis.'

The Secondary Period.—This period is characterized by the appearance of generalized symmetrical eruptions of the skin and mucous membranes, visceral inflammations, and sometimes anæmia, fever, headache, neurasthenia, and other nervous affections. It is generally announced by the appearance of the roseola rash on the trunk, but may begin with general symptoms of malaise, insomnia, headache, and cold extremities.

Anæmia is sometimes very marked, especially in women, and there is a diminution both in oxyhæmoglobin and in the number of red corpuscles. In severe cases there may be leukæmia, and in extreme cases pernicious anæmia. Leucocytosis of the cerebro-spinal fluid has been found by Widal, Ravaut, and others, in cases of secondary syphilis with nervous symptoms, headache, etc.

Headache with nocturnal exacerbations is a characteristic feature of syphilis, and may occur at an early period, with or without periostitis of the cranial bones. It may be mistaken for *migraine*, and is sometimes so severe as to cause delirium. The syphilitic headache may be due to periostitis, meningitis, or arteritis.

Other secondary syphilitic manifestations are: neuralgic pains, affecting chiefly the sciatic, intercostal, and cranial nerves; nocturnal pains in the bones, due to periostitis; arthralgia and hydrarthrosis of the joints; tenosynovitis and myositis; jaundice, gastralgia, and enteritis; general adenopathy, affecting especially the suboccipital and anterior and posterior cervical glands; laryngitis; alopecia; amenorrhœa and dysmenorrhœa in women.

More severe affections may occur, usually during the later secondary period. These include iritis and irido-choroiditis, keratitis; arteritis causing early cerebral and spinal syphilis; nephritis; glycosuria and diabetes; hæmoglobinuria; enteritis, epididymitis, otitis, etc. These affections are described later on in the chapters dealing with the various systems of the body.

The chief points in the diagnosis of secondary syphilis are the roseolar rash, mucous patches and erythema in the throat, mucous patches or condylomata on the genital organs, enlargement of the suboccipital and cervical glands, acneiform papules on the scalp with general alopecia, and the remains of a chancre with its satellite glands.

Syphilitic Fever.—It has been erroneously stated that syphilis is an apyretic disease, and this belief has no doubt led to some cases of mistaken diagnosis. That a variable degree of pyrexia is not uncommon in secondary syphilis was pointed out long ago by Fournier, who divides syphilitic fever into two classes—symptomatic and essential.

The *symptomatic* fever accompanies the outbreak of cutaneous eruptions, and cases have been mistaken for aberrant measles or small-pox.

The *essential* form of syphilitic fever occurs independently of cutaneous lesions, and is more common in women. It

usually appears from the third to the eighth month of the disease, and may assume an intermittent or continuous type.

The *intermittent type* is characterized by daily nocturnal rises of temperature unaccompanied by rigors. It differs from *malarial ague* in the absence of the regular sequence of cold, hot, and sweating stages, in the absence of the enlarged spleen, in the attacks being nocturnal instead of diurnal, and in reacting to mercury, but not to quinine.

The *continuous type* is less common than the above, and generally lasts only a few days. In some cases, however, it persists for several weeks, and is accompanied by prostration and an adynamic condition resembling typhoid. To this form Fournier has given the name of *syphilitic typhose*. The chief points in which syphilitic typhose differs from typhoid are the absence of the characteristic temperature chart, the enlarged spleen, iliac pain, diarrhœa, dry glazed tongue and delirium of typhoid. The blood is also negative to Widal's agglutination reaction. Nevertheless, as the majority of practitioners are unacquainted with syphilitic fever, it is possible for such cases to be mistaken for subacute attacks of typhoid, especially as the appearance of a few syphilitic papules may suggest typhoid spots. This mistake in diagnosis is all the more liable to occur because the patient is not likely to attribute an attack of fever to syphilis or to mention the existence of the latter to the medical man he consults for his fever.

Varieties of Secondary Syphilis.—Fournier subdivides secondary syphilis into five types—medium, mild, severe, nervous, and recurrent.

The *medium* or average type is characterized by the association or succession of the following symptoms: roseola; papular syphilides on the trunk and limbs, scalp, and palms of the hands; acneiform eruption on the scalp; slight temporary alopecia; cervical adenopathy; headache and periosteal pains in the limbs; mucous patches in the mouth.

The *mild* type is simply an attenuation of the preceding, in which the eruptions are more erythematous than papular. Mucous patches in the mouth are almost invariably present,

and sometimes constitute the sole manifestation. In about 5 per cent. of cases the secondary symptoms may be so mild as to escape the patient's attention. This fact accounts for a certain number of cases of *syphilis ignota*.

The *severe* form is characterized by more intense and often confluent eruptions, sometimes assuming the form of tertiary cutaneous affections; ulcerations of the mucous membranes; laryngitis; iritis; onyxis and perionyxis; extensive alopecia; periostitis and joint affections; fever of the typhose type; severe headache; anæmia and disturbances of general nutrition. This type is a transition form between ordinary secondary syphilis and malignant syphilis.

The *nervous* type is confined almost exclusively to women, and consists in the association of a series of nervous manifestations with the specific symptoms. The principal of these are general nervous erethism, neuralgic pains, asthenia, mammary and dorso-metacarpal analgesia, algidity, hyperidrosis, cardiac arythmia, boulimia, hysteria, etc. In fact, this type appears to be constituted by syphilitic infection occurring in a hysterical or neurotic subject, and acting as an exciting cause on a predisposed subject.

The *recurrent* form is one in which there is a tendency to the repeated recurrence of comparatively mild lesions, chiefly erythematous syphilides of the roseolar type (recurrent roseola) and buccal mucous patches. According to Fournier, these recurrences may take place several times, even as late as the eleventh year of the disease. These cases usually occur in patients who have been treated with mercury (*vide* Late Secondary Syphilides, p. 75).

The Tertiary Period.—The characteristic features of the tertiary period of syphilis are: (1) The more circumscribed and less symmetrical distribution of the lesions; (2) their non-resolvable nature as compared with the resolvable lesions of the secondary period; the former tending to fibrous organization or fatty degeneration, while the latter tend to undergo resolution; (3) the rarity of contagion and transmission to the fœtus.

Although these attributes apply to the majority of tertiary

syphilitic lesions, they must not be accepted in an arbitrary manner. In the first place, there is no sharp pathological distinction between secondary and tertiary lesions; secondly, there is no definite time limit between secondary and tertiary manifestations, for contagious lesions having the appearance of secondary syphilides have been observed ten or fifteen years after infection; and lesions of a tertiary nature may appear in the first or second year of the disease.

All that is known at present is that at a certain period in the evolution of the disease the specific microbe undergoes some kind of modification, and may remain latent for an indefinite period. It may, however, manifest renewed activity after lying dormant for a long time, as is shown by the occurrence of outbreaks of tertiary syphilis accompanied by general symptoms, indicating a revival of the infective process.

The recent discovery of the *Spirochæta pallida* in gummata shows that tertiary lesions may sometimes be contagious. 'In tertiary syphilis everything shows the presence of a pathogenic agent, no doubt modified, attenuated, but always active, the manifestations of which, in spite of certain differences, remain comparable to those of the secondary period. The most recent researches have only shown us the rarity of the *Spirochæta pallida* in tertiary syphilis' (Balzer).

According to Fournier's statistics, tertiary lesions are most frequent in the second, third, and fourth years, after which date they gradually become less common, and are rare after the twentieth year. The maximum is in the third year, but cases are not uncommon in the first year. Fournier mentions cases in which tertiary lesions appeared thirty, forty, and even fifty years after infection, but these might possibly have been due to reinfection at a more recent date (p. 45).

Tertiary lesions often assume a uniform type, and may repeat themselves in the same organ or tissue several times. The following table, taken from Fournier, shows the relative proportion of tertiary syphilis of the different organs, based on 4,400 cases. From these figures we see that the nervous system is the most often affected by tertiarism (1,851 cases), and after this the skin (1,418 cases):

MANIFESTATIONS OF TERTIARY SYPHILIS.

Cutaneous syphilides	1,418	
Subcutaneous gummata	202	
The genital organs	271	
The lips	42	
The tongue	262	
The soft palate	215	
The fauces	23	
The pharynx	94	
Different mucous membranes	8	
The osseous system	519	
The nasal bones and hard palate	229	
The nose	43	
The joints	22	
The muscles	16	
The tendons	3	
The digestive tube	8	
Ano-rectal lesions	12	
The larynx and trachea	32	
The lung	23	
The heart	7	
The arteries	15	
The liver	9	
The kidney	30	
The testicle	245	
The urethra	10	
The eye	110	
The ear	26	
The brain	758	
Cerebro-spinal lesions	9	
Monoplegia	6	
The spinal cord	136	
Tabes	628	
Cerebro-spinal tabes	45	1,851
Neuritis and muscular atrophy	24	
General paralysis	86	
Ocular paralysis	110	
Facial hemiplegia	23	
Divers nervous affections	6	
Other lesions	17	

Causes of Tertiarism.—The chief cause of tertiary manifestations appears to be inadequate mercurial treatment during the primary and secondary stages of the disease; for, according to

Fournier's statistics, out of 100 cases of tertiary syphilis, 78 had been incompletely treated, 19 had received average treatment, and 3 only had been properly treated. The details are shown in the following table of 2,396 cases (Fournier).

No treatment at all	197
Mercurial treatment less than three months	490
,, ,, ,, six ,, ...	399
,, ,, ,, twelve ,, ...	594
,, ,, for one year	146
,, ,, for one to two years	357
,, ,, for two to three years	98
,, ,, for three years	34
,, ,, for more than three years	29
Iodide treatment only	45
Treatment by sarsaparilla, etc.	7
Total	2,396

It also appears from Fournier's statistics that about 90 per cent. of tertiary lesions follow secondary syphilis of a more or less benign character. This is probably explained by the fact that patients with mild secondary symptoms are less likely to persevere with their treatment than those suffering from severe secondary syphilis.

Other etiological factors in tertiarism are: traumatism; overwork, mental or bodily; excesses of all kinds, especially alcoholic; tuberculosis, anæmia, and other debilitating conditions. Traumatism may excite an outbreak of tertiary syphilis, especially in the form of periostitis following an injury to the bone. Alcohol has been called 'the born enemy of syphilis,' and there is no doubt that chronic alcoholism associated with syphilis forms one of the worst possible pathological combinations, often leading to chronic disease of the arteries and all its effects.

Contagion.—Both the chancre and secondary lesions are contagious, and the mucous patch is probably the lesion which is responsible for most syphilitic contamination. Tertiary lesions are usually regarded as non-contagious; but this idea requires some modification, for Neisser, Finger, and Land-

steiner have produced chancres in monkeys by inoculation with the peripheral parts of gummata, showing that tertiary lesions are inoculable before they have undergone caseation or secondary infection. In the present state of our knowledge contagious syphilitic lesions contain the *Spirochæta pallida.*

In 1860 Pellizzari proved that the blood was contagious by inoculating a medical man, who volunteered for the purpose, with the blood of a woman with secondary syphilis. In this case a chancre appeared on the twenty-fifth day, and was followed by secondary symptoms.

It was formerly believed that the natural secretions—milk, sweat, saliva, mucus, urine, and semen—were not contagious unless mixed with syphilitic discharges; but there is no reason why secretions, whether morbid or natural, which are derived from diseased blood should not themselves be contagious. Assuming the *Spirochæta pallida* to be the pathogenic microbe of syphilis, the secretion from any glandular cells in which this organism has been found is likely to be contagious. Levaditi, who has found the spirochæte in the renal epithelium of syphilitic infants, suggests that the urine may even convey contagion.

With regard to the *semen*, this was for a long time held to be non-contagious, chiefly owing to the negative results obtained by Mireur. This observer (1876) inoculated fresh semen, obtained from a man with untreated secondary syphilis, on four persons who were free from syphilitic antecedents, in each case with a negative result. Quite recently, however, Finger has shown by experimental inoculation of monkeys with syphilitic semen that the latter can convey contagion.

This fact also proves the possibility of parental transmission of syphilis to the fœtus through the semen, a question which has hitherto been the subject of much unnecessary controversy.

A positive result was obtained by inoculating a girl with *milk* from a syphilitic woman by Voss of St. Petersburg. It would be advisable, therefore, to regard both the morbid and natural secretions of a syphilitic subject as possibly contagious.

Vaccinal Syphilis.—Several epidemics of syphilis caused by vaccination from syphilitic infants have occurred in former

times, before calf lymph became generally used; the best known of these epidemics occurred at Lupara and Rivalta. It was thought at first that the lymph only conveyed the syphilitic contagion when mixed with blood; but it has been proved that the lymph itself, free from admixture of blood, may be contagious both during the active and latent periods of syphilis.

Modes of Contagion.—Syphilis is in most cases contracted from a syphilitic sore on the genital organs during sexual connection, but a considerable number of contaminations are caused accidentally (*syphilis insontium*) by kissing persons with syphilitic sores in the mouth, by using contaminated drinking-vessels, spoons, towels, water-closets, etc. (*vide* Extra-genital Chancres p. 59). Contagion may thus be venereal or non-venereal, direct or indirect. A healthy woman may even act as an intermediary agent of transmission from one man to another by means of syphilitic semen or discharges deposited in the vagina. In the same way a healthy wet-nurse may contaminate a healthy infant after having given the breast to a syphilitic suckling.

Whether a breach of surface is necessary for contagion is uncertain, but it is probable that a minute abrasion occurs in most cases. It is quite possible, however, for the virus to gain entry into the duct of a cutaneous gland and penetrate into the blood without a breach in the epidermis.

Malignant Syphilis.

Although there is a difference of opinion as to the definition of malignant syphilis, it is best to regard it as a type in which ulcerative lesions develop at an early period. That is to say, it is a type in which the secondary period appears to run on into the tertiary without the usual intervention of a latent period. In this way ulcerative lesions of a rapidly destructive nature appear a few months after infection, and are mingled with papular syphilides of the secondary type. There is usually a considerable degree of anæmia and cachexia, and often fever (syphilitic typhose). The lesions of malignant syphilis do not

react well to mercury, and its administration sometimes has to be suspended.

According to Fournier, alcohol, paludism, mental and bodily depression, are all predisposing causes for malignant syphilis, but cases sometimes occur in persons apparently in robust health.

The prognosis is grave, on account of the condition of cachexia and exhaustion, or by the development of cerebral or visceral lesions. Malignant syphilis (*syphilis maligna*), which is characterized especially by the early development of ulcerative lesions and general cachexia, must be distinguished from severe syphilis (*syphilis gravis*), which is characterized by dangerous localization of the disease, or by association with other morbid conditions.

The cause of malignant syphilis is doubtful; it has been attributed both to excessive virulence of the microbe and to secondary infection with other organisms. It would appear more probable that it is due to the implantation of the microbe on virgin soil—*i.e.*, on persons whose ancestors have been free from syphilis.

Exotic Syphilis.

Syphilis is found in nearly all tropical countries, with the exception of regions not yet open to commerce, where the natives have not come in contact with the white man. The journals of Captain Cook show that his sailors brought syphilis into Polynesia. According to Jeanselme, there are still certain regions free from the disease, including Central Africa and New Guinea; but such regions are rapidly diminishing, and in the near future syphilis will reign over all parts of the globe. This absence of syphilis in certain regions is not due to immunity to the disease, but simply to absence of contact.

The gravity of syphilis depends to a great extent on race. In the African negro the disease is relatively benign, and the same is true of yellow fever; hence, in the Congo syphilis has not taken on the severe character it usually assumes in regions recently open to commerce. In Madagascar, on the other hand, the disease is severe; however, this island is not

peopled by negroes, but by Asiatics who have formerly drifted there. The Malays swarming on the eastern coasts convey it from place to place, and in all these countries, under different climates, syphilis has the same characters.

The origin is often extragenital, owing to the exposed skin being affected with insect bites and abrasions, and it is possible that insects frequently convey the infection. Syphilis of the Far East differs from that of Europe in usually assuming the early malignant type, and in the chancre being usually phagedenic. Secondaries are less apparent in the coloured races and buccal lesions rare. An early rupial syphilide which extends rapidly and deeply over the body and limbs is common. Osteo-arthritic manifestations with severe nocturnal pains are frequent. Periostitis of the femur, tibia, clavicle, radius, and ulna often occur, and the joints are distended with effusion, crippling the patient like acute rheumatism. Later on enormous gummatous placards may decorticate a whole limb or destroy the eyelids, nose, and ears. The repair of these lesions causes deformity and contractions resembling those produced by burns. The articular ends of the bones are altered, and mutilation of the hands and feet and pseudo-elephantiasis often occurs.

'This tertiary syphilis,' says Jeanselme, 'with multiple and disseminated manifestations, which is often complicated with phagedena, causes profound disorganization of the skin and skeleton, gives rise to incurable mutilations, but rarely causes death. It owes this relative benignity to the constant integrity of the mucous membranes and viscera.'

Perforation of the palate is rare; tertiary glossitis, orchitis, and hepatitis are almost unknown; and the eyes are never affected. The nervous system is seldom attacked, and tabes and general paralysis are unknown. These peculiarities are possibly due to the absence of alcoholism, and to the mode of life involving less strain on the nervous system. In Japan tabes and general paralysis are said to have appeared since the adoption of European customs and manners.

Hereditary syphilis is frequent, and again affects chiefly the skin and bones. The most common signs are the saddle-nose,

sabre-tibia, and deformities of the cranium. The teeth are seldom affected, and keratitis is rare. The nervous system of the fœtus being more vulnerable than that of the adult, hydrocephalus, congenital spastic paraplegia, and idiocy are not unknown.

Syphilis contracted by Europeans from natives usually runs the same course as in Europe, but may be more severe. Jeanselme mentions the case of a soldier with a phagedenic chancre destroying nearly the whole penis; a vast rupial ulceration of the thigh and hemiplegia thirty-five years later. Two comrades, who contracted the disease from the same woman, also had phagedenic chancres.

Syphilis and Yaws.

The chief disease from which tropical syphilis has to be distinguished is *yaws* (parangi or pian), which has by some been regarded as itself a form of tropical syphilis. Yaws resembles syphilis by its reaction to mercury and iodide, and by its osteo-arthritic phenomena. It differs from syphilis in the following points: (1) It is not hereditary; (2) it is auto-inoculable; (3) the skin lesions are monomorphous; (4) in the absence of scars, alopecia, and lesions of the viscera and mucous membranes (these, however, are rare in tropical syphilis); (5) in the first lesion being of the same nature as the secondary ones; (6) in the absence of endo- and peri-arteritis in the lesions. Moreover, syphilis can be inoculated in the subjects of yaws, as was done experimentally by Charlouis, and syphilitic subjects may contract yaws.

The typical eruption of yaws is a raised red excrescence rising abruptly from the skin and covered with a scab. This applies to both the primary sore and to the successive crops. There are no early throat lesions as in syphilis, and the late pharyngeal ulceration sometimes seen in yaws may be due to superadded syphilis. Yaws is common in infancy, but rare in the first year, and not accompanied by changes in the teeth or keratitis (these, however, are usually absent in tropical syphilis).

Daniells remarks that 'it is quite inexplicable, on the

hypothesis that yaws and syphilis are the same disease, that in widely different races living in one part of the colony syphilis may assume the peculiar features called yaws, while the same races in another part of the colony, living under exactly similar climatic conditions, present the ordinary features of syphilis, and not those of yaws.' According to Daniells, yaws in British Guiana is confined to a few districts, where it attacks both negroes and East Indians, while syphilis is common throughout the colony. Yaws only attacks those who mix with the natives.

Although all this evidence tends in favour of syphilis and yaws being distinct diseases, it is necessary to note that a spirochæta, apparently identical with the *Spirochæta pallida*, has been found in yaws by Castellani. Three forms of spirochæta were found by this observer, and were examined by Schaudinn himself, who stated that one of them closely resembled the *Spirochæta pallida*. Other bodies were also found by Castellani, who regarded them as developmental stages in protozoa. If spirochætes are the causal agents of both syphilis and yaws, the two diseases may be allied, and yaws may possibly be a modified form of tropical syphilis.

Phagedena.

Phagedena may be defined as a progressively destructive form of ulceration, of a rodent or 'gnawing' type, relatively or absolutely rebellious to treatment, varying in duration, and sometimes indefinitely chronic.

Phagedena may occur in association with primary syphilitic chancre, simple chancre, or tertiary syphilitic lesions, but is more common in the last. It attacks venereal sores more frequently than others, but also occurs in malignant ulcerations, lupus, tropical ulcer, and certain cachectic ulcers.

Tertiary Phagedena.—The most common situations for tertiary phagedena are the genital organs, nose, and throat. Sometimes subcutaneous and submucous gummata become phagedenic when they perforate the skin. It presents at first the usual characters of tertiary syphilitic ulceration, covered with rupial crusts; but later on it loses its original features

and resembles phagedenic ulceration due to other causes than syphilis. Extension may take place in two ways—(1) superficially, in a more or less circinate or serpiginous manner; (2) deeply, perforating the subcutaneous tissue, fascia, muscles, and bone. The nerves, vessels, and aponeuroses resist the destructive action longer than the softer tissues.

Etiology. — Phagedena is predisposed to by all causes which diminish the powers of resistance of the organism, such as starvation, overwork, tubercle, alcoholism, malaria, etc.; but it sometimes occurs in persons apparently in robust health. Tertiary phagedena may be partly due to the absence of proper antisyphilitic treatment during the early stages, to the use of irritating applications, to the irritation caused by urine and other discharges, and to conditions such as phimosis and paraphimosis.

Carmichael attributed phagedena to a special virus apart from syphilis, on the strength of phagedenic chancres contracted by several men from the same woman. Sperino, however, showed that the same virus inoculated in different persons produced an ordinary chancre in some cases and a phagedenic chancre in others. It has also been observed that different chancres, both simple and syphilitic, occurring in the same individual may have a tendency to become phagedenic. These facts point to the nature of the soil as an etiological factor in the production of phagedena.

It is probable that both the nature of the soil and the virulence of the contagion contribute to the occurrence of phagedena, and that it is more likely to occur in a person whose ancestors have been free from syphilis, or in a person who has been inoculated with virus derived from an individual of another race. This explanation will apply to cases of malignant syphilis, in which phagedena is often a feature, and to severe epidemics of syphilis, such as the outbreak at Naples at the end of the fifteenth century.

Diagnosis.—Tertiary phagedena differs from phagedenic simple chancre in the presence of gummatous infiltration; in the circinate outline; in being more often penetrating than superficial in its progress; in the absence of the bacillus of

Ducrez; in the absence of a phagedenic bubo, which is always due to simple chancre.

Termination.—Tertiary phagedena may end in resolution in a few weeks, or may become chronic and persist for years. Sometimes it causes death by cachexia or by hæmorrhage, but occasionally it may last for a long time without affecting the general health.

It may cause considerable mutilation and deformity by destruction of the genital organs, nose, lips, and throat, and may lead to atresia of the urethra, vagina, naso-pharynx, anus, and palpebral fissures. Extensive necrosis of bone may also result, chiefly affecting the tibia and bones of the skull.

Treatment.—Iodides should be given in large doses, but mercury should be used with caution, especially in cachectic cases. Local treatment consists in prolonged antiseptic baths, iodoform, and mild antiseptic dressings. Caustics or the thermo-cautery are contra-indicated except as a last resource in very chronic cases.

Diagnosis and Prognosis.

The diagnosis of syphilis should be based on the association of certain manifestations rather than on any single sign or symptom. It is often unwise to base a diagnosis of syphilis on a single lesion unless this is corroborated by other evidence of the disease. This is especially important in the case of cutaneous syphilides, the diagnosis of which often depends on the presence of other signs of syphilis.

As regards anamnesis, or 'history,' the patient's statements are often misleading, and exposure to syphilitic contagion is often wilfully denied. In some cases where the chancre has consisted only of an insignificant abrasion, or where the secondary eruptions have been slight, the patient may not even be aware that he has had syphilis. This is especially the case in women, and is known as *syphilis ignota*. It is therefore useless to depend on a history of syphilis as an aid in the diagnosis of a doubtful lesion, and all such cases should be given a trial with mercurial treatment. This procedure is known as the *therapeutic test*. In women, however, valuable

evidence is obtained by the history of previous pregnancies, a series of *abortions* or *miscarriages* being almost certain evidence of syphilitic infection.

The diagnosis of the different syphilitic manifestations is given in the following chapters. It is hardly necessary to state that the diagnosis of syphilitic lesions has been considerably facilitated by the discovery of the *Spirochæta pallida*, which we may assume for the present to be the specific microbe of syphilis.

Prognosis.—The prognosis of syphilis must always be reserved, because of the possibility of the later development of *parasyphilitic affections*. The majority of cases, when well treated, apparently remain free from symptoms afterwards. Fournier states that only about 5 per cent. of patients who have undergone prolonged treatment suffer from severe symptoms, and consequently that in 95 per cent. of cases the disease runs a comparatively benign course. It also appears from Fournier's statistics that out of 100 cases of tertiary syphilis, only three had undergone proper treatment. It is necessary to point out that this proper treatment means a course of *at least three years' duration*, so that we may take it for granted that the great majority of syphilitic subjects are not sufficiently treated, and this no doubt accounts for the frequency of many diseases which are the outcome of syphilis. The prognosis, therefore, depends chiefly on the *duration of treatment*.

The chief difficulties in forming statistics of the prognosis of syphilis are (1) its excessively long duration; (2) the multiplicity of its manifestations. For instance, a patient may consult a syphilologist for primary or secondary syphilis, and afterwards, when he develops some affection of the eye or the nervous system, will consult another specialist in one of these departments; the syphilologist, not seeing the patient again, may include him in the list of cures.

No idea of the future course of the disease can be gathered from the nature of the chancre; for, although severe and phagedenic forms of chancre may be followed by severe secondary eruptions, tertiary syphilis may follow chancres of the most

benign character. As Fournier remarks, 'the present, in syphilis, is in no way the mirror of the future.'

The prognosis of syphilis is aggravated by various secondary factors: alcoholism; intercurrent diseases, such as tuberculosis, malaria, etc.; mental and bodily overwork; fatigue, starvation, etc. The combination of syphilis and chronic alcoholism is a potent factor in the causation of arteriosclerosis, chronic interstitial nephritis, and cirrhosis of the liver. This subject will be dealt with later on, and the prognosis of syphilis as it affects life-assurance and marriage are discussed in a separate chapter.

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CHAPTER III

PATHOLOGY

All syphilitic lesions—primary, secondary, and tertiary—consist essentially in an interstitial infiltration of embryonic cells, constituting an inflammatory neoplasm or *granuloma.* This inflammatory neoplasm is distributed especially around the small bloodvessels, and is of *perivascular origin.* In every syphilitic lesion the bloodvessels are affected with *endo-periarteritis* and *endo-periphlebitis.* The *Spirochæta pallida* has been found in the walls of the vessels, and is especially abundant in the perivascular cell infiltration. The capillaries are dilated and surrounded by exuded cells.

The inflammatory neoplasm, or *syphilitic granuloma,* undergoes resolution in the case of the chancre and secondary syphilitic lesions, but in tertiary lesions it tends both to *fibrous organization* and *necrobiosis,* with caseous and gummatous alterations. Hence, although the morbid process is fundamentally the same in all stages of the disease, tertiary lesions have a characteristic clinical appearance, owing to this tendency to sclerosis and necrobiosis.

The Syphilitic Granuloma (Syphiloma).

This consists of round cells, epithelioid cells, and giant cells, thus resembling other inflammatory granulomata, such as tubercle and glanders. The round cells are of several types—polynuclear leucocytes, lymphocytes, embryonic connective-tissue cells, and plasmatic cells (*plasmazellen*). The *plasmatic cells* form the greater part of every syphilitic neoplasm. They are larger than leucocytes, oval or polyhedral, without processes,

granular and easily stained, and with an excentric nucleus. The epithelioid cells are said to be plasmatic cells in a state of degeneration. The giant cells are formed either by coalescence of several plasmatic cells or by subdivision of the nucleus. The origin of the plasmatic cells is disputed; Unna regards them as derived from the connective-tissue cells, but most observers consider them to be derived from white blood-corpuscles.

The plasmatic cells, including a variable number of epithelioid and giant cells, are grouped round the bloodvessels in the form of irregular sheaths, which are characteristic of syphilitic lesions. Accumulations of these cells can sometimes be seen by the naked eye as round white spots the size of a pin's head. These are known as *miliary gummata* or *elementary syphilitic nodules*. Agglomerations of these give rise to larger gummata, which may attain considerable dimensions.

The naked-eye appearance of tertiary syphilitic lesions of the viscera shows a meshwork of fibrous bands intersecting the whole or part of the organ, and connected usually with fibrous thickening of its capsule. In the meshes of the fibrous bands are found gummata of various sizes, appearing as opaque yellow masses on section, sometimes hard, at other times caseous. Each *gumma* is surrounded by a fibrous capsule, with ramifying processes connected with the fibrous bands, and sometimes by a zone of sclerosed parenchymatous tissue of the affected organ. In some cases concentric zones can be seen—an outer zone of fibrous tissue, a zone of plasmatic cells, and a central mass of cells undergoing caseous degeneration. The caseous matter is composed more of albuminoids than fatty granules. Caseous gummata are more liable to soften and break down when they are subcutaneous or periosteal, or when they occur in an organ possessing an external outlet, such as the lung.

The caseation of gummata is probably due to a combination of causes: (1) Obliteration of vessels, (2) excessive crowding of cells, (3) direct action of the virus.

Parenchymatous Changes.—Apart from the damage to the cells by vascular obliteration and compression of fibrous

bands caused by syphilitic lesions, the syphilitic virus must now be regarded as having a direct action on the cells themselves. Darier has shown that in the case of early syphilitic nephritis the cells of the uriniferous tubules undergo granular changes before there is any proliferation of connective tissue. Again, in the so-called 'white pneumonia' of heredo-syphilis there is proliferation of the epithelial cells of the pulmonary alveoli, as well as of the connective-tissue stroma; the same with the hepatic cells in cases of syphilitic *icterus gravis* and probably also with the cells of the nervous system in cerebro-spinal syphilis. The direct action of syphilis in the parenchymatous cells is also supported from the recent researches of Levaditi, who has found the *Spirochæta pallida within the cells* in various organs.

To sum up. The morbid changes caused by syphilis are as follows:

1. Endo-periarteritis and endo-periphlebitis, leading to obliteration of vessels and consequent ischæmia or necrobiosis of the parts supplied.*

2. Inflammatory granulomatous infiltration, tending to the ormation of diffuse interstitial fibrosis or localized gummata; or more often a combination of both in the form of *sclero-gummatous lesions*.

3. Direct action on the parenchymatous cells.

Diagnosis of Syphilitic Granuloma.—The syphilitic granuloma resembles in many respects the granuloma of tuberculosis, and to a lesser extent those of lepra, glanders, and mycosis fungoides. In mycosis fungoides, however, the vascular changes are absent, and in glanders they are much less marked. In lepra growths in the viscera occur resembling gummata, but the bacillus of Hansen is always present. With regard to tubercle, the resemblance is much closer, and it is sometimes difficult to distinguish between syphilitic and tuberculous lesions, especially as there may be a combination of both in the same patient.

The chief differences are that the tubercular granuloma has a greater tendency to soften and cause destruction of tissue,

* See Chapter VI. for further details.

and a less tendency to fibrous organization, than the syphilitic granuloma. The vascular changes are also less marked than in syphilis. The discovery of the tubercle bacillus and positive inoculation of the guinea-pig will decide in favour of tuberculosis.

Darier remarks: 'The distinction between these two kinds of infiltration, which is sometimes very difficult, can hardly be based on the nature of the elements which compose them, because they are the same. It is based on their relative proportions, on the degree and mode of alteration of the stroma. In most cases of lupus, for example, the giant cells and epithelioid cells are more abundant and grouped in the centre of follicles formed of small plasmazellen; the stroma is distinct from the infiltration, which penetrates it little, but which replaces and absorbs it. In the syphilides, on the contrary, the degenerated cells are more scanty and more disseminated; the distribution of the neoplasm, formed of large plasmatic cells, is rather perivascular than nodular; it infiltrates between the meshes of the stroma, which often tends to sclerosis more than absorption.'

Schaudinn has recently found the *Spirochæta pallida* in the peripheral part of a gumma of the liver in the twelfth year of syphilis.

Parasyphilis.

The syphilitic microbe, besides its direct action on the blood-vessels and connective tissue, which gives rise to the ordinary syphilitic lesions, has a toxic effect on the cells themselves which leads to degenerative changes. These degenerative effects, or sequelæ, of syphilis are known as parasyphilitic, metasyphilitic, postsyphilitic, or as quaternary syphilis.

The term 'parasyphilis,' introduced by Fournier, is the one in most general use, although in some cases the designation *quaternary syphilis* would appear more suitable. Fournier defines parasyphilitic affections as 'a series of morbid manifestations which, although they have nothing syphilitic in nature, are none the less syphilitic in origin, in that they are born of syphilis and produced by its existence, and in all probability would not be produced without it.' These affections are numerous, and are characterized by being not necessarily

of exclusive syphilitic origin, and by not reacting to anti-syphilitic treatment.

Parasyphilis does not result from the direct action of the microbe, but rather from the action of syphilotoxins, or by *toxalbumins* arising from the modified tissues. The syphilotoxins appear to have a special affinity (chemotaxis) for certain tissues, especially the nervous system.

Parasyphilitic affections may be divided into three classes: (1) Functional disorders, such as neurasthenia and hysteria; (2) permanent lesions of the nature of sclerosis and atrophy, such as tabes, general paralysis, leucoplasia buccalis, and arterio-sclerosis; (3) degenerations, including constitutional degeneration of the individual, often leading to tuberculosis, diabetes, etc., physical and mental decay; the dystrophic effects of heredo-syphilis, or heredo-parasyphilis.

The definition of parasyphilis as given by Fournier appears to be too arbitrary, and there is no real reason why any sharp distinction should be made between syphilis and parasyphilis. In face of the definition that parasyphilitic lesions are not syphilitic in nature we have the fact that tabes, which is generally regarded as the type of parasyphilitic diseases, is second in frequency among the tertiary lesions of syphilis. This would seem to show that our ideas of the nature of syphilitic lesions require expanding, a point which Fournier pointed out at the discussion on general paralysis at the Academy of Medicine (Chapter XI). Secondly, the reaction to anti-syphilitic treatment is simply a matter of degree. Mercury will only cause the absorption of comparatively young syphilitic lesions, and has no effect on a patch of sclerosis or on an obliterated artery; neither will it regenerate atrophied cells.

Among the parasyphilitic affections Fournier includes the following:

In Acquired Syphilis:

The pigmentary syphilide (*vide* p. 78).
Hystero-neurasthenia.
Tabes and general paralysis.
A special form of epilepsy.
A special form of muscular atrophy.
Leucoplasia buccalis.

In Hereditary Syphilis:

General dystrophic disorders.
Arrest of development, both physical and mental.
Malformations.
Infantilism and dwarfism.
Hydrocephalus.
Rickets.
Some cases of early meningitis.
Some cases of epilepsy.
Juvenile tabes and general paralysis.

Hermanides, in his exhaustive work on parasyphilis, adds the following to this list:

Diabetes.
Alopecia areata.
Cheloid.
Arterio-sclerosis.
Chronic interstitial nephritis.
Amyloid degeneration.
Tuberculosis.
Sarcoma, and possibly carcinoma.

It is necessary to say that Hermanides guards his statements by admitting other causes than syphilis for these diseases; 'All these affections may develop more or less frequently on another etiological soil than syphilis.'

With regard to most of these affections, we must agree that syphilis is probably a frequent, if not the most common cause. Syphilis is certainly one of the most important factors in the production of arterio-sclerosis, and is a strong predisposing cause to tuberculosis and cancer. If the inclusion of sarcoma and carcinoma among the parasyphilitic affections appears to be transgressing the limits of pathological knowledge, we must admit that no other satisfactory explanation of the origin of malignant tumours has yet been brought forward. Further research for parasitic protozoa in these diseases may throw more light on the subject.

As Fournier remarks: 'I do not think I am going too far in predicting that certain pathological conditions, the intimate nature of which is not yet elucidated, and the syphilitic origin

of which may remain subject to controversy, will some day take their place beside the types which I have at present mentioned.'

Bacteriology.

It has for some time been assumed that syphilis is a microbial disease, but all attempts to discover a pathogenic microbe were inconclusive, till in 1905 Schaudinn and Hoffmann discovered a special form of protozoon in syphilitic lesions, to which they gave the name of *Spirochæta pallida*. Although it has been found impossible to cultivate this organism, its constant presence in primary and secondary syphilitic lesions, and in the lesions of hereditary syphilis, appears to show that in all probability it is the pathogenic agent of syphilis.

Previous to this discovery, different organisms had been claimed by several observers as the microbe of syphilis, but none of them have been confirmed by subsequent investigation. The principal claimants were Klebs, Lustgarten, Van Niessen, Jullien and De Lisle, Max Joseph and Piorkowski.

That the pathogenic agent of syphilis was a protozoon was first suggested by Doehl, Schuller, and Horand, and later by Siegel, who has recently described a protozoon in syphilitic lesions which he names the *Cytorrhyctes luis*. It is possible that this organism may represent a developmental stage of the *Spirochæta pallida*.

The Spirochæta Pallida, or Treponema Pallidum.—This is a very delicate, mobile spiral organism, varying in length from 4 to 14 μ (on the average about the diameter of a red blood-corpuscle), and about $\frac{1}{4}$ μ in thickness.

It differs from the *Spirochæta refringens*, which is found on the surface of lesions of the genital organs, by its smaller size, less refractive power, greater difficulty in staining, and by the greater number of the turns of the spiral (eight to twenty-six), which are narrow and corkscrew-like. A characteristic feature of the *Spirochæta pallida* is that it maintains the spiral form both in motion and at rest, while the coils of other spirochætes are more shallow when at rest.

The *Spirochæta pallida* usually stains a pink colour with

PLATE II.

PLATES II. AND III.—SECTIONS OF ORGANS FROM CASES OF FŒTAL AND HEREDITARY SYPHILIS, SHOWING THE SPIROCHÆTA PALLIDA. STAINED BY LEVADITI'S METHOD WITH SILVER NITRATE. ZEISS $\frac{1}{12}$ IMMERSION OBJ., OC. NO. 6.

FIG. I.—SECTION OF LIVER FROM MACERATED FŒTUS.

v, Portal vessel, containing cellular débris (*g*) and spirochætes (*s'*); *p*, wall of vessel infiltrated with spirochætes (*s'''*); *s*, spirochætes in the vascular endothelium; *h*, group of hepatic cells altered by maceration and containing spirochætes (*s''*).

pallida is the causal agent of syphilis, and goes so far as to regard syphilis as a *chronic relapsing spirillosis*. 'If in a case free from syphilis a spirillum is found having from ten to twenty-four narrow spirals, which is coloured pale rose by Giemsa, and which presents other characters of the *Spirochæta pallida*, this will in no way affect the etiological importance of this microbe in syphilis, but will only prove that there exist different spirilla very similar in their microscopic appearance, just as the bacilli of tubercle and leprosy have a remarkable resemblance to one another when they are examined stained under the microscope.'

The only fact wanting to prove the pathogenic nature of the *Spirochæta pallida* is the absence of cultures, all attempts at culture having failed in the case of spirochætes, spirilla, and trypanosomes. However, experimental inoculation of monkeys, with the reproduction of lesions in series containing the spirochæte, furnishes an argument the value of which is almost equivalent to that of cultures.

The reason why the *Spirochæta pallida* has not been observed before in syphilitic lesions is explained by the difficulty in technique, and also by the fact that it is not always found. Metchnikoff failed to find it in 26 per cent. of the cases he examined. Thus, a negative examination does not prove that a lesion is non-syphilitic, any more than the absence of the tubercle bacillus in lupus negatives the tuberculous nature of this affection.

The researches of Levaditi have shown that the *Spirochæta pallida* is present in the walls of the bloodvessels, and especially around them, but that it is rarely found in the blood itself. This shows that the organisms are conveyed by the blood, but that the blood is not the medium in which they develop. They would appear to multiply in the walls of the vessels and penetrate thence to the connective tissue and parenchymatous cells of the different organs. The presence of spirochætes within the cells of the liver, suprarenal glands, and sweat glands shows that the syphilitic process is not exclusively confined to the bloodvessels and connective tissue, but that there may be a direct action of the virus on the cells themselves.

That the organism reacts by *phagocytosis* against the spirochætes is shown by the presence of these micro-organisms within large mononuclear cells in cases of 'white pneumonia' in the syphilitic fœtus. In some cases the spirochætes were found in a degenerate condition, manifested by irregular undulations and moniliform swellings, and were finally reduced to granules.

Examination of preparations for the Spirochæta pallida requires a practised eye and a high magnifying power (Zeiss $\frac{1}{12}$, immersion lens), and several preparations may have to be examined before the organism is found. Hoffmann, in examining the scrapings of fourteen chancres, arrived at a positive result eight times after a minute and a half's observation, three times after two to five minutes, once after fifteen minutes, the remaining two cases requiring more than an hour.

Rille and Vockerodt have noticed that the spirochætes are often found attached to the red blood-corpuscles.

The number of spirochætes varies considerably in apparently similar lesions, and also in different parts of the same lesion, so that simultaneous preparations made with the same technique contain them in very different proportions. Hence the necessity for examining a number of preparations before concluding that the spirochæte is absent.

The spirochæte may be examined in scrapings from chancres and syphilitic lesions, or in sections. (For staining methods, see Appendix.) In the case of chancres a doubtful diagnosis may be cleared up by finding the spirochæte in the exudation. For this purpose the surface of the chancre should be lightly scraped with a vaccination lancet, or similar instrument, to avoid hæmorrhage, till colourless exudation appears. This liquid contains the spirochætes in greater number than the surface secretion of the chancre.

Levaditi and Petresco have demonstrated the presence of the spirochætes in artificially-produced blisters in the neighbourhood of cutaneous syphilides. This fact may be useful in certain cases of doubtful diagnosis, although a negative result was obtained in cases of recent roseola.

Action of Mercury on the Spirochæta Pallida.—Levy Bing has

shown that this organism rapidly disappears under the influence of mercury. Six or seven days after an injection of gray oil the spirochætes became scarce, and a week after the second injection they had almost disappeared. Kowalewski, after demonstrating the presence of spirochætes, noted their disappearance after six injections of sublimate.

Protozoology of the Spirochæta Pallida.—The spirochæta of syphilis is a *flagellate protozoon*, and must be distinguished from the *spirilla*, which are forms of bacteria. The names *Treponema pallidum* and *Spironema pallidum* have been suggested as being more correct than *Spirochæta pallida*, but the latter, having appeared first, is so far in more general use.

The microbe of syphilis thus belongs to the group of parasitic protozoa known as the Trypanosomidæ, which includes four genera: Spirochæta, Treponema, Trypanosoma, and Trypanoplasma.

It is interesting to note that spirochætes have been described in the lesions of *yaws*, or *pian*, a disease which in many respects resembles syphilis (*vide* p. 21). Again, the *dourine*, or 'mal de coit,' of horses is now known to be caused by a trypanosome, and the discovery of a parasitic protozoon in this disease has been urged as proving that it is distinct from syphilis, which it resembles in some of its clinical aspects. However, the argument is now reversed in the light of recent research in the causal agent of syphilis; and if both syphilis and dourine are caused by members of the same class of parasitic protozoa, it is possible that the two diseases may be allied.

Another point of interest lies in the possibility of syphilitic infection through the medium of insects, which are known to convey other forms of trypanosomiasis, such as sleeping sickness.

According to Maclennan, the *Spirochæta pallida* represents one phase only in the life-history of a protozoon. This observer has found certain minute spherical bodies associated with the spirochæte in the same preparations. These bodies, which resemble *Leishmann-Donovan bodies*, rather than the *Cytorrhyctes luis* of Siegel, are often found with tails, and intermediate stages are described between the spherical form and

the spirochæte. Maclennan therefore regards the spirochæte as only one stage in the life-history of the micro-organism of syphilis.

The protozoology of the *Spirochæta pallida* cannot, therefore, be regarded as definitely settled; but if the tailed bodies described by Maclennan are really stages in the development of the spirochæte, the analogy with trypanosomes is still closer. The tailed form of the Leishmann-Donovan body was shown by Dutton to be a connecting-link with the trypanosomes, and it is possible that syphilis may be regarded, not as a chronic relapsing spirillosis, as Metchnikoff suggests, but as a form of trypanosomiasis.

Experimental Inoculation in Apes.

In 1903 Metchnikoff and Roux proved that syphilis was inoculable in animals by inoculating a chimpanzee with material from a human syphilitic chancre of a month's duration. Some years previously Martineau and Hamonic had inoculated certain monkeys, but as these were of the lower catarrhine species, the results were inconclusive. Inoculation was performed by small superficial scarifications on the eyebrows, eyelids, and genital organs.

The researches of Metchnikoff, Roux, and Neisser show that the *chimpanzee*, which is more closely allied to man zoologically than other species, such as the gorilla or orang-outang, develops syphilis to a degree more resembling human syphilis than that obtained by inoculation of other species of monkeys. The chimpanzee is therefore the best animal for experimental purposes.

Metchnikoff and Roux have inoculated twenty-two chimpanzees, with positive results in every case. In this species the first incubation stage varies from fifteen to forty-nine days, averaging thirty days. The second incubation period varies from nineteen to sixty-one days, averaging thirty-three days. The primary lesion appears as a small rose-coloured, slightly raised papule, which in a few days becomes covered with small squames. After a few days the papule develops into a charac

teristic indurated chancre, with induration and enlargement of the corresponding lymphatic glands. The primary lesion in the chimpanzee thus corresponds in all respects with that of man. In the chimpanzee the chancre is followed by secondary syphilis, which is manifested by papular and ulcerative syphilides of the skin, mucous patches of the mouth, alopecia, and palmar syphilides. As a rule, the chancre and the secondary lesions disappear spontaneously in the course of a few weeks; but in some cases the animals die from secondary infection of extensive ulcerative syphilides. In no case were tertiary lesions observed. The syphilitic nature of the secondary lesions was proved by inoculation in other chimpanzees, with resulting chancres. Histological examination of the lesions showed periarteritis and other characteristics of syphilitic lesions.

In the lower catarrhine monkeys, the *macaques* and *papions*, experimental syphilis is limited to the chancre, and no secondary symptoms occur. These animals may therefore be used for the attenuation of the syphilitic virus, or for control purposes. Metchnikoff concludes that the attenuation of the syphilitic virus, in order to obtain an antisyphilitic vaccine, must be made by passage through the lower catarrhine monkeys, such as the *Macacus rhesus*.

Thibierge and Ravaut have obtained constant results in the case of the *Macacus sinicus* and *cynomolgus*. These investigators inoculated in every case the free border of the eyelid, a situation less exposed than other regions to the risk of secondary infection and trauma. They explain the inconstant results obtained by others to the fact that other regions of the body, such as the genitals, were sometimes inoculated.

The chief object of their investigations was to prove whether the macacus would react constantly to the syphilitic virus in the same way that the guinea-pig does to tubercle, and in this they were successful, as the macacus reacted in every case.

The incubation of the chancre was twenty-three days on the average, and the lesion appeared first as an œdematous infiltration of the border of the eyelid, soon becoming a copper-

coloured nodule, which was followed by desquamation. There was no ulceration, only very slight erosion; no appreciable induration, and no adenitis. The chancre was not followed by secondary lesions.

Histological examination of the lesion showed the presence of perivascular cell infiltration, formed by lymphocytes and plasmatic cells, and in some cases arteritis was seen.

The inoculation chancre in the macacus thus corresponds in evolution and structure to human chancre, but differs in the absence of induration and adenitis. This is due to the chancre being pure and free from the effects of secondary infection. It shows the distinction between the lesions proper to syphilis and those due to secondary infection and irritation. The chancre is probably the only syphilitic lesion in the macacus, and the absence of secondary phenomena shows the resistance of these animals to syphilis. As Metchnikoff and Roux pointed out, monkeys are more refractory to syphilis the further they are removed from the anthropoid. That the chancre in the macacus is really syphilitic was proved by the latter observers by inoculation of the chimpanzee.

Thibierge and Ravaut obtained positive results with inoculation from chancres and mucous patches; also from a bullous heredo-syphilitic lesion. Inoculation with cerebro-spinal fluid giving the reaction of lymphocytosis in cases of secondary and hereditary syphilis was negative. Also, it may be mentioned that Widal and Ravaut did not find the spirochæte present in the cerebro-spinal fluid in cases of active syphilis.

These inoculations were made in a group of animals of which one only was free from previous inoculation, and this one only reacted and developed a chancre. This showed that positive inoculation conferred immunity which lasted a year.

Control experiments were made by inoculation with the secretions of the genital organs containing various microbes, but they were all negative except from syphilitic lesions. In one animal a single inoculation from a 'mixed chancre' gave rise to an ulcerative lesion, due to the bacillus of Ducrey, followed on the thirtieth day by the syphilitic chancre.

Thibierge and Ravaut conclude that 'in the species of monkeys on which we have experimented the primitive lesion determined under the conditions we have mentioned, although reduced to a minimum, is sufficiently characteristic to be recognised with certainty as soon as it appears.' The constancy of their results is important, and appears to show that the macacus monkey (*sinicus* and *cynomolgus*) can be used as a test for syphilis in the same way as the guinea-pig is used as a test for tuberculosis.

Metchnikoff and Roux have shown that immunity in monkeys is not established till some days after inoculation. Human virus inoculated eighteen days after inoculation of a chimpanzee with virus from a macaque produced a chancre. This experiment confirms the results obtained by Queyrat in auto-inoculation in man (p. 53).

Experiments in Serotherapy.

Since the researches of Richet and Héricourt many attempts have been made to prepare antisyphilitic serums, but only with negative results. Metchnikoff and Roux have undertaken an elaborate series of researches with a view to obtaining a more active serum from the less receptive species of monkeys, such as the macaques. Monkeys were chosen not only because they are inoculable with syphilis, but also because they furnish a serum which has very little hæmolytic action on the human red corpuscles. The following is a brief summary of their results.

1. Attempts at serotherapy in the chimpanzee failed completely, although the injections of serum were commenced from the day of inoculation. Injections were made with the serum of macaques inoculated with syphilitic virus, and then treated for several months with repeated injections of the blood of syphilitics in the secondary stage.

2. In another series of experiments the serum of macaques immunized as above was applied, not by injection, but in the form of dried powder applied to the point of inoculation. The results were inconstant.

3. Inoculation of a chimpanzee with virus previously mixed

in vitro with the serum of immunized macaques gave no conclusive result, owing to the premature death of the animal.

4. Attempts at immunization with virus attenuated by heating to 48° C., and also with matter from human gummata, had no preventive effect, for the chimpanzees treated by these methods contracted syphilis in the usual way when inoculated afterwards.

It therefore appears that the syphilitic virus is very fragile, and soon loses its vitality outside the body. It loses its virulence when heated to 48° C. and when dried. Also, it does not traverse porcelain filters. Klingmuller and Baermann, in order to test the activity of the filtered virus, were bold enough to inoculate themselves with the filtrate from syphilitic tissues after passage through a Berkefeld filter. The result was negative.

Metchnikoff's latest remarks on the subject (International Congress of Medicine at Lisbon, April, 1906) are that up to the present attempts at antisyphilitic serotherapy in the monkey have not given satisfactory results, and that possibly better results may be obtained if it is found possible to cultivate the *Treponema pallidum in vitro*.

Neisser, who has recently conducted experimental inoculation of monkeys on a large scale in Java, comes to the following conclusions :

In the first place he points out the fallacy of assuming that the syphilis of the lower apes is attenuated because the external signs are limited to the chancre, and secondaries are absent. He has shown that positive inoculations can be made from the organs of lower monkeys which have no signs of secondary syphilis. 'It is obvious that if we do not know all the facts concerning the true state of the *normal* disease in the infected monkeys, we can say nothing of the so-called modifications in the course of the infection, either by the employment of a virus modified in any way, or by the application of a method having the object of influencing the animal before or after infection ; that is to say, by a method of immunization or by treatment. Taking this point of view as a basis—and for us syphilographers it is indispensable—I must admit that *all efforts made to discover*

a method by immunization or by treatment have been in vain. It is true that differences in the incubation and evolution of the chancre have been noted, but these modifications are absolutely without value, because it is not the symptoms which interest us, but the disease as a whole. I believe, on the contrary, that it is only the *quantity* of spirochætes inoculated, and not the *quality* of their virulence, which exerts an action on the rapidity of development of the primary lesion. Again, the success and rapidity of inoculation depend on the nature and age of the syphilitic product employed.'

On examining the internal organs of infected lower monkeys Neisser found that inoculations could often be made with the spleen and bone-marrow of orang-outangs, but not from lower monkeys. This shows that the virus was only contagious for the anthropoids (chimpanzee) and not for the lower monkeys. So far this is the only fact that proves that there is an *attenuation of the virus*, and this attenuation is only produced in the internal organs, not in the chancre of the same monkey. On the other hand, chimpanzees can be inoculated easily from the products of the lower monkeys. Hence, attenuation is not the rule, and it is possible that the passage of the virus through several monkeys, the orang-outangs especially, may increase the virulence of the virus instead of diminishing it.

As regards attempts at *immunization* Neisser concludes that 'we have not obtained a *serum* sufficiently strong to protect animals against syphilitic infection, nor a method which can confer active immunity, because we have not yet produced a truly attenuated virus, either by passage through an intermediate animal, or by any chemical or physical method. The virus is either quite dead, or it produces the usual chancre. But perhaps, even with the chancre which appears to us normal, we may have modified the general course of infection, so that the disease may take a more favourable course than when it is produced by a normal virus. It therefore appears that in the whole study of experimental syphilis it is this question of generalization, its beginning and its duration, which must be studied at each step' (International Congress at Lisbon, April, 1906).

Prophylactic Experiments.

Attempts at serotherapy having given disappointing results, Metchnikoff and Roux next tried preventive treatment by the local application of mercury to the point of inoculation. Repeated experiments on chimpanzees and macaques showed that inunction practised at the point of inoculation an hour or an hour and three-quarters after introduction of the virus, with mercurial ointment, or an ointment of 10 parts of calomel with 20 of lanoline, prevented the development of the disease.

These experiments showed that the virus of the first inoculation is destroyed by mercury, without giving rise to any immunity against subsequent inoculation. The experiment was performed subsequently on a medical student who was willing to offer himself as a martyr to science. Inoculation was made in scarifications on the balano-preputial furrow, and the point of inoculation rubbed for a few minutes with calomel ointment (1 in 3) an hour afterwards. No signs of syphilis appeared in the student up to three months afterwards, nor in a macaque treated in the same way; but chancres developed in the ordinary way in other monkeys inoculated with the same virus and not treated with calomel ointment. The calomel ointment is preferable to the ordinary mercurial ointment, as it is less irritating.

This important result led to the investigation of the length of time during which the virus remains localized to the point of inoculation. The ear of a macaque was inoculated and the part inoculated removed, and by this means Metchnikoff and Roux determined that the period of localization of the virus is at least twenty-four hours.

Neisser's results, however, do not confirm those of Metchnikoff, and he points out the uncertainty of the result in any given case. In a macaque, in which the part was excised *eight hours* after inoculation, syphilis developed in the normal way, while another monkey, in which excision was performed *twelve days* after inoculation, remained healthy. With regard to inunction with calomel ointment an hour after inoculation, Neisser's results were not all successful, and he remarks

that possibly the scarifications were made more superficially in Metchnikoff's cases. He also points out that if a *positive* result of inoculation shows the presence of the syphilitic virus, a great many experiments are necessary to demonstrate its *absence*.

Reinfection.

It was for some time taught that syphilis could only be acquired once in a lifetime, and that reinfection was impossible, but a number of cases have been recorded by careful observers which seem to establish the possibility of reinfection beyond a doubt. It is true, as Fournier has pointed out, that if the diagnosis of the second infection is based on the chancre only, such cases may in some instances be explained away as being pseudo-chancres (p. 120) or chancriform gummata (p. 174). It is also possible that cases of recurrent roseola and other late secondary syphilides occurring many years after the first infection may have been mistaken for evidence of reinfection; but it might also be argued that some such cases are really due to reinfection, and not to recurrent secondary outbreaks.

In order to establish the fact of reinfection, it is necessary for two distinct attacks of primary and secondary syphilis to have been seen in the same patient by the same observer, or proved by satisfactory documentary evidence. Several cases fulfilling these conditions have been reported. Hutchinson has observed two cases, in one of which the patient passed through two attacks of primary and secondary syphilis, with an interval of five years; in the second case the patient is said to have had three attacks, with intervals of fourteen and nine years. Berkeley Hill relates the case of a surgeon who acquired syphilis in the usual way; eleven years later he contracted a digital chancre, followed by secondary syphilis.

Diday, in 1862, published twenty-seven cases of reinfection, but in fourteen of these the second attack was limited to an indurated chancre, and two occurred while tertiary symptoms of the first attack were present; in three cases the first contagion is reported as consisting of chancre only. In eight cases only are secondary symptoms mentioned as occurring in the secondary contagion.

Gascoyen, in 1875, reported eleven cases, in which secondary syphilis occurred in six and an indurated chancre only in four; in the eleventh case the first attack consisted of a chancre only. He also collected sixty published cases, including the twenty-seven of Diday's, thirty-five of which were followed by secondary syphilis. In five cases the supposed chancre of reinfection occurred while tertiary symptoms were still present.

A considerable number of cases of reinfection have been since published, many of which must be accepted as genuine. Mansell Moullin has recorded a case in which the interval between the two attacks was only two and a half years.

The possibility of reinfection shows that the immunity conferred by the first attack is of uncertain duration, and probably depends on many factors, such as the quality of the disease, the resisting power of the patient, and the effect of treatment, etc. It is also possible for the patient to be suffering from the effects of both attacks at the same time, for parasyphilitic effects, such as tabes or general paralysis, due to the first attack, may appear after the date of reinfection. This may explain some of the cases in which active syphilitic lesions have been found in tabetics or general paralytics, and which have been urged by some authors as evidence in favour of tabes and general paralysis being syphilitic rather than parasyphilitic in nature.

Reinfection in Hereditary Syphilis.—It is an interesting point how far hereditary syphilis confers immunity against the acquired disease. Tarnowski has published a considerable number of cases in which reinfection with the acquired disease occurred in the subjects of hereditary syphilis. To this he gives the name of 'binary syphilis,' and considers that this combination has a more lethal effect than the hereditary disease by itself on the offspring of such subjects.

The latest contribution to this subject is by Rostaine, who concludes that the descendants of syphilitics, although never having had signs of the hereditary disease, may contract syphilis in the usual way, even when the father has syphilitic lesions after their birth. Hence there may be descendants of uncured syphilitics who are not themselves syphilitic. He

quotes cases observed by Boeck and Taylor, in which reinfection occurred in hereditary syphilitic subjects. He also mentions the idea which is prevalent among the public, and among many medical men, that hereditary syphilis confers permanent immunity, and quotes a case of Tarnowski where the patient refused to take mercury because his father confessed to him that he had had syphilis.

The duration of immunity conferred by hereditary syphilis is not known, but is stated by Finger to cease at about the age of puberty. It may be concluded that it confers immunity while in an active condition, but allows of reinfection in proportion to its attenuation.

It is interesting to note that Ricord in his later years recognised the possibility of reinfection. In a letter to W. Acton in 1872 he said: 'Now that we have authentic examples of fresh contagions of indurated chancre, with consecutive evolution of the whole series of constitutional symptoms, this proves that patients have been cured, just as the possibility of contracting small-pox afresh or of vaccination again taking proves that the first variolous or vaccine influence has ceased.'

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CHAPTER IV

CHANCRES

THE initial lesion of syphilis, or *hard chancre*, constitutes the primary period of syphilis. The syphilitic chancre (primary sclerosis, or Hunterian chancre) is also called the infecting chancre, to distinguish it from *soft or simple chancre*, which is a local venereal lesion quite distinct from syphilis.

The *incubation period* of syphilitic chancre after infection is about three or four weeks. Fournier gives the minimum at fifteen days and the maximum at forty-two days, and considers that cases of earlier or later appearance of the chancre which have been reported are open to question. It must be borne in mind that the date of the infectious coitus is not necessarily the date of infection of the organism; for instance, the virus might remain for a time under the prepuce before penetrating into the lymphatics.

In the experimental inoculation of syphilis in a healthy man by Pellizzari the first signs of the chancre appeared on the twenty-fifth day, and in Metchnikoff's inoculations of the chimpanzee the chancre appeared on the twenty-sixth day. The average incubation period of syphilis may therefore be fixed at about *twenty-five days*.

The syphilitic chancre commences as a *papule*, the fragile epidermis of which soon becomes eroded by friction. The erosion is therefore secondary, and by protecting the part, as was done in certain inoculations in monkeys (p. 39), this erosion does not occur. The essential lesion is therefore a papule, not an erosion, and still less an ulcer. Ulceration of the chancre is caused by secondary infection.

The chancre, when first seen in the human subject, usually

presents itself as a superficial flat erosion with no definite borders. It is circular or oval in form, deep red in colour (the colour of muscular tissue), later on grayish in the centre, exuding a thin sanious discharge, and sometimes covered with a thin diphtheroid membrane. When this pellicle is detached, there is oozing of dark red blood from the surface. In a few days the base of the chancre becomes *indurated*, and this induration, which is a characteristic feature, may assume a discoid or a nodular form. At this stage, when the chancre is taken between the fingers, it feels like a piece of cartilage inserted in the skin.

It is necessary to bear in mind, however, that the induration may be absent, or, at any rate, so slight as to be inappreciable. On the other hand, the base of a simple soft chancre (non-syphilitic) may become indurated by inflammatory thickening. In diagnosing between hard and soft chancre, therefore, too much weight must not be given to the question of induration, and the other objective characters must be depended upon.

Histologically, the chancre is formed by a process of small-celled infiltration and hyperplasia of connective-tissue cells, constituting the *plasmoma* (Unna). Epitheliod cells and giant cells are also present. The small arterioles and veins are affected with *peri-* and *end-arteritis* and *peri-* and *endo-phlebitis*, and this process is almost always continued along the coats of the vessels beyond the limits of the chancre (Cornil). 'The chancre is nothing more than a dermic papule with dense cell infiltration, supported by a fibrillary meshwork; with intense lesions of the bloodvessels, sometimes extending to obliterative sclerosis; also, thickening with vacuolation and exulceration of the Malpighian layer, and often œdema and lymphangitis' (Balzer).

For the first four days the chancre forms an insignificant erosion with no characteristic feature by which it can be diagnosed. After attaining maturity it remains stationary for two or three weeks, and then heals, leaving a brownish scar which gradually disappears. In other words, the chancre has a *tendency to spontaneous cure*.

The induration always remains after the surface has healed,

and may persist for several weeks or months. It is then important as an aid in retrospective diagnosis. During the reparative process the surface of the chancre loses its grayish tint and varnished appearance, and assumes the red aspect of an ordinary sore. Sometimes the chancre becomes ulcerated by secondary infection and irritation, and may then leave a permanent scar after healing, but as a rule the chancre leaves no scar.

The total duration of the chancre from its first appearance to its final cicatrization is, in uncomplicated cases, only four to six weeks.

Adenopathy.—About a week after the appearance of the chancre, the lymphatic glands corresponding to the region in which the chancre is situated begin to enlarge, and constitute what is called the *satellite bubo.* In the case of chancre of the genital organs the bubo is situated in one or both groins. Sometimes the bubo is on the opposite side to the chancre, owing to the crossing of the lymphatic glands in the middle line.

The affected glands are hard, indolent, painless, and freely movable, rarely exceeding the size of a nut or olive. The overlying skin is unaltered and not adherent to the glands, which feel like nuts under it. This group of enlarged glands secondary to the chancre was known by the name of the 'pleiads of Ricord.' Suppuration never occurs in syphilitic bubo unless there has been infection of the chancre with pyogenic micro-organisms. These enlarged and indurated glands always persist for some time after the chancre has disappeared, and are therefore useful as an aid to diagnosis.

Diagnosis of Syphilitic Chancre.—During the first four days, before induration and bubo have developed, the chancre cannot be diagnosed from a simple erosion.* Moreover, after cauterization with silver nitrate or carbolic acid, etc., a simple erosion may simulate syphilitic induration.

Herpes.—Some varieties of herpes, such as confluent herpes or solitary herpes, have a resemblance to the early stages of

* Diagnosis may now be made by the presence of the *Spirochæta pallida.*

syphilitic chancre. But herpes as a rule is generally multiple, whereas chancre is usually single. Herpes is often preceded by burning and itching sensations, which are absent in the case of chancre. If a typical vesicle of herpes is found, diagnosis is rendered less difficult, but it must be borne in mind that *herpes may coexist with chancre.*

The chief characteristic of the herpetic lesion is its *polycyclic outline*, consisting in the coalescence of segments of small circles. The outline of the chancre, on the other hand, is circular or oval.

Scabies.—The lesions of scabies are common on the penis, and, as a matter of fact, scabies may be regarded as a venereal disease, since it is often contracted by sexual intercourse. The lesions consist in circular erosions or subulcerations, covered with a thin scab. The base may be indurated to a certain extent by inflammatory infiltration, and the glands in the groin may be enlarged. Under these conditions the sarcoptic sores have a close resemblance to syphilitic chancres.

Fournier mentions a case of scabies in which four exactly similar lesions occurred on the penis; three of these disappeared under treatment for scabies, but the fourth developed into a hard chancre.

Simple or Soft Chancre.—The chief points in the differential diagnosis of hard and soft (syphilitic and non-syphilitic) chancres is shown in the following table:

	Soft Chancre.	Syphilitic Chancre.
1.	Generally multiple.	Rarely multiple.
2.	Consists of a punched-out ulcer, with sharp-cut edges and an irregular base.	Consists of an erosion, with smooth surface and no sharp edges. Rarely a true ulceration.
3.	Yellow colour.	Red or gray colour.
4.	Purulent discharge.	Sero-sanious discharge.
5.	Base soft or inflammatory.	Base indurated.
6.	Bubo inflammatory.	Bubo hard and indolent.
7.	Auto-inoculable.	Not auto-inoculable.
8.	Pus contains the bacillus of Ducrey.	
9.	Incubation nil.	Incubation three or four weeks.

Some of these points require further consideration.

1. *Auto-inoculation.*—The simple chancre is auto-inoculable, and produces a similar sore at the point inoculated. The syphilitic chancre, when mature, is not auto-inoculable—that is to say, it does not reproduce another chancre when inoculated in the same subject, but only gives rise to a pustule, if it has any result at all. However, positive cases of auto-inoculation from very young chancres have been reported, and it is possible that another chancre may be reproduced before the organism has become immune to syphilis. In other words, immunity takes a certain time to develop. Queyrat has recently shown that auto-inoculation of the syphilitic chancre gives positive results during the first eleven days which follow its appearance.

2. *Incubation.*—The incubation period of syphilitic chancre, as mentioned previously, is three or four weeks, while the simple chancre has practically no incubation period, since it develops almost immediately after inoculation. The period of incubation is, however, seldom of much use in diagnosis, since patients have usually had several connections, any one of which might have given rise to contagion.

Mixed Chancre.—It is possible for both simple chancre and syphilitic chancre to coexist, and either may be inoculated on the other. If the syphilitic virus is inoculated at the same time and at the same point as the simple chancre, a hard chancre will appear in the spot formerly occupied by the simple chancre. Inversely, a soft chancre may be inoculated on the top of a syphilitic chancre, resulting in a chancre with an indurated base and ulcerated surface—the so-called 'mixed chancre.'

The simultaneous presence of the bacillus of Ducrey and the *Spirochæta pallida* in mixed chancre has been demonstrated by Thibierge, Ravaut, and Lesourd.

Varieties in Syphilitic Chancre.—In atypical or abortive chancres the characteristic signs may be wanting—even induration. 'Induration does not constitute syphilis, but syphilis constitutes induration' (Fournier).

The syphilitic chancre is usually single, but sometimes multiple. When multiple, there are seldom more than two or three, but Fournier had a case in which no less than

twenty-three chancres occurred on the two breasts of a woman, due to contagion by suckling; also Ricord mentions a case in which nineteen chancres appeared on the penis and scrotum.

The usual size of the syphilitic chancre is that of a split pea or a sixpence, but sometimes it attains the size of a shilling or two-shilling piece. Occasionally it becomes tuberous and ulcerative, and may then simulate an epithelioma (hypertrophic chancre).

Varieties in the Male.—Chancre situated on the surface of the glans penis is flat, with a lamellar induration; chancre situated in the balano-preputial furrow is more raised and papular, with nodular induration at the base. Other lesions, such as simple chancre or herpes, when situated in the balano-preputial furrow, also have a tendency to inflammatory induration, owing to the richness of the part in lymphatics. The syphilitic chancre in this situation is sometimes surrounded by secondary satellite indurations.

Chancre of the *meatus* may occur on one or both lips, and may extend into the urethra. It may be erosive or ulcerative, and bleeds easily. There is always considerable induration. In its early stages it may be mistaken for a gonorrhœal erosion. Chancre of the meatus is more liable than others to phagedena.

Chancre of the *urethra* is not very rare, but is often missed. It generally occurs near the meatus, and is accompanied by some pain on micturition and a sero-sanious discharge. It may be felt as a hard lump in the urethra by pressing the latter from before backwards.

Chancre of the *prepuce* is often ragged, owing to friction, and is liable to become inflamed and cause phimosis.

A chancre may cause *phimosis* in three ways: (1) By infiltration of the prepuce; (2) by setting up balano-posthitis; (3) by lymphangitis and œdema of the prepuce. In this way *concealed chancres* are produced. In diagnosing concealed chancre, the induration must be felt through the prepuce, and the glands in the groin must be examined. In doubtful cases the prepuce may be slit up, or circumcision performed.

Chancres in Women.—The labia majora are the commonest

situations for chancres in women, and in Fournier's statistics they occurred there in 114 out of 249 cases. The next situations in order of frequency are the labia minora, the fourchette, the cervix, the clitoris, the vaginal orifice, and the urethra.

Chancre of the *labia majora* is papular, erosive or ulcerated, and distinctly indurated; chancre of the *labia minora* is more erosive and less indurated; chancre in the *vagina* is rare, and forms a small erosion with little induration. The rarity of chancre in the vagina may be due to the elasticity of the walls or to the absence of glandular orifices; but it is possible that some escape detection by being concealed in the vaginal rugæ.

Chancre of the *cervix uteri* occurred 13 times out of 249 cases in Fournier's statistics. It has a tendency to rapidly spontaneous cure, which may account for its being not more frequently observed. Chancre of the cervix may be situated on one or both lips, or may surround the external os. It forms a flat grayish-red erosion, with a purple areola.

The adenopathy affects the pelvic glands, which cannot be felt; but in some cases of chancre of the cervix enlarged glands have been felt in the groins, which can only be explained by the anastomosis of the lymphatics of the cervix with those of the vagina.

Diagnosis has to be made from cervical erosion, herpes, and simple chancre.

Cervical erosion radiates from the os and extends into the lower lip of the cervix; it is red and granular, with a mucopurulent discharge, and is of slow evolution. Cervical chancre is generally eccentric, and not prolonged into the cervical canal; it is of a gray colour and of more rapid evolution.

Herpes sometimes occurs on the cervix, but may be recognised by its polycyclic border.

Simple chancre, when single, or when several are fused together, may resemble syphilitic chancre; but they differ in their yellow colour and sharp-cut edges, and by the fact that simple chancres are usually present about the vulva.

Chancre of the cervix occurring in the late stages of pregnancy may cause obstructed labour.

Successive Chancres.—Cases have been observed in which successive chancres appeared at intervals of a few days. Fournier mentions a case of three successive chancres, the third of which appeared fifteen days after the first.

That successive chancres may be caused by several contaminations has been shown experimentally. Hence immunity of the organism takes several days to develop. Cases have been reported in which a successive chancre developed as late as twenty-five days after the first; but there are many possible errors in diagnosis, such as erosions due to balanitis, herpes occurring round a chancre, or eroded satellite lymphatic infiltrations, which sometimes occur near the original chancre.

The successive chancre is not necessarily smaller than the first (aborted), for Lesné had a case of four chancres of the face, the last of which was the largest of all.

Complications of Chancre.—The chief complications of syphilitic chancre are inflammation and phagedena.

Inflamed chancre may be caused by dirt and the decomposition of retained secretions under a phimosed prepuce, or by excessive cauterization. The chancre becomes red, swollen, and painful, and may end in sloughing. Œdema, lymphangitis, and adenitis are set up, and a suppurating bubo may develop in the groin. Balano-posthitis and paraphimosis are other complications which may follow. In the female, œdema of the labia may become hard and form a swelling which persists for some time.

Phagedena.—According to Fournier, phagedena occurs more frequently in simple than in syphilitic chancre. It may occur in a gangrenous or in an ulcerative form. The former consists in the formation of successive sloughs, which are detached progressively and gradually form an excavation. The ulcerative variety of phagedena consists in a molecular necrosis of the tissues, forming a deep red ulceration with a red areola and sanious discharge. The phagedena of syphilitic chancre differs from that of simple chancre on the one hand, and tertiary syphilitic phagedena on the other hand, by being more localized. It does not extend to the surrounding parts or

become serpiginous. It may be complicated by hæmorrhage, stricture of the meatus, or perforation of the urethra. Occasionally it gives rise to phenomena of septic infection; but this is rare.

The *etiology* of phagedena is obscure. It may occur after infection from a benign case of syphilis, so that the quality of the contagion has little to do with it. Sometimes it occurs in debilitated and alcoholic patients, and in some cases it is due to diabetes; but there is often no appreciable cause.

The *prognosis* of phagedenic chancre is bad, because it signifies an indefinable inherent malignancy, and is generally followed by early and severe secondary symptoms, or by malignant syphilis. This only applies to the immediate sequelæ, for there is no relation between the severity of tertiary lesions and the nature of the chancre. The most benign chancre may be followed by the most severe tertiarism.

Redux or Relapsing Chancre.—After cicatrization the chancre occasionally undergoes a retrograde metamorphosis which may take one or two forms—(1) it may ulcerate afresh, constituting the *redux chancre;* (2) it may soften in the centre, forming the *pseudo-gummatous chancre.*

The *redux chancre* usually resembles the original, and occurs a few days after healing. It generally follows chancres in which the induration has been abundant. Sometimes a second relapse occurs. The redux chancre is contagious like the original.

The *pseudo-gummatous chancre* is more rare, and is formed by a softening of the centre of the induration remaining after cicatrization of the original chancre. This discharges a yellow sanious liquid by one or more orifices, through which the detritus of the induration is evacuated. Both these conditions are different forms of the same morbid process, the first being a superficial ulceration, the second a central softening.

Chancriform Gumma.—Certain forms of gumma of the penis, called by Fournier the *tertiary chancriform syphiloma*, closely resemble chancre. The differential diagnosis is given in Chapter IX.

Ablation of the Chancre.—With a view to cause the

abortion of syphilis many measures have been tried, including cauterization and excision of the chancre, and excision of the glands as well. All these measures have failed to prevent secondary syphilis. Most of the 'successful' results reported were probably cases of simple chancre.

Brandes excised a chancre ten hours after its appearance without preventing secondary syphilis. Further, the point of inoculation has even been excised before any chancre appeared, with a view to prevent syphilis; but this also failed (Mauriac).

Local Treatment of Chancre.—As the chancre has a spontaneous tendency to heal, little treatment is required, except cleanliness and asepsis. Cauterization of any kind is to be condemned, as it often sets up inflammation; in doubtful cases it also masks the diagnosis for a time. Daily washing with 1 in 2,000 perchloride of mercury solution, followed by the application of calomel cream (calomel 1 part, lanoline and vaseline 10 parts), is sufficient in most cases. If there is much exudation, a dusting powder of zinc, starch, and talc may be applied.

If the chancre becomes *inflamed*, frequent tepid baths and wet boracic dressings are indicated.

The treatment of *phagedenic chancre* is important, as any form of cauterization is contra-indicated. The proper treatment is by tepid antiseptic baths two or three times a day, prolonged for two or three hours. An ordinary hip-bath is sufficient for the purpose, and the best medicaments to add to the bath are creolin or iodine (sufficient tincture of iodine to make the water the colour of pale sherry). After carefully drying the chancre, it should be dusted with iodoform and dressed with absorbent boracic wool.

Here I may say a few words on the so-called *substitutes for iodoform*. Their name is legion, and each new one which appears is advertised as superior to all its predecessors. It is true most of them avoid the unpleasant smell of iodoform, which is the main object in view, but their efficacy disappears in proportion to the loss of the objectionable odour. I have tried most of them, sometimes comparing them with iodoform

on multiple sores in the same patient, but they are all of them vastly inferior to iodoform. Professor Fournier also comes to the same conclusion, and refers to them as 'a veritable deluge of pharmaceutical novelties which pretend to dethrone iodoform, emanating from laboratories with less scientific than mercantile aspirations.'

Cases of *concealed chancre* with phimosis require irrigation, by a small catheter inserted under the prepuce, with lotions of 1 in 2,000 perchloride of mercury or silver nitrate (1 to 2 per cent.). Some cases require circumcision.

Extragenital Chancres.

Extragenital chancres form nearly 10 per cent. of all chancres (Fournier). They have been found on almost every part of the body, except the soles of the feet; but, after the genital organs, the lips and mouth are the most common situations for chancres.

In Fournier's statistics of 1,124 cases of extragenital chancre, no less than 567 were situated on the lips.

Buccal Chancres.—Syphilis may be conveyed to the mouth in many different ways: (1) By *genito-buccal* contagion; (2) by *buccal* contagion from kissing; (3) by *mediate* contagion through the agency of contaminated instruments and utensils, such as spoons and forks, glasses, pipes and cigarettes, pen-holders, paper-knives, toys, speaking-tubes, money, etc., and surgical instruments, such as tongue depressors, dental instruments, Eustachian catheters, etc.

Two well-known examples of syphilis derived from buccal contagion are—(1) *glass-blower's syphilis*, conveyed by the custom of handing the glass-blowing tube from mouth to mouth; (2) *infection of sucklings* from a chancre on the nipple of the wet-nurse.

Labial Chancre.—Chancre of the lip is usually single, occasionally double, and is more common on the lower lip. It may form a simple erosion, or may become covered with a brown scab; in the latter case it may be mistaken for herpes, eczema, or impetigo. In some cases it develops into a large

papule resembling a malignant growth. The main points of difference between this hypertrophic form of labial chancre and epithelioma are shown in the following table:

Labial Chancre.	Labial Epithelioma.
1. Surface smooth and sometimes varnished.	Surface irregular and ragged, or sometimes vegetating.
2. No distinct borders.	Raised, thickened, and everted borders.
3. Surface does not bleed.	Bleeds easily on the slightest contact.
4. Glands soon become enlarged, and attain their maximum in the second or third week.	No enlarged glands till the fourth or fifth month.
5. Evolution complete in about three weeks.	Evolution takes several months.

The *glands* affected in labial chancre are the *submaxillary*, and, contrary to the general rule of primary syphilitic adenopathy, these glands often become acutely inflamed and may suppurate. This fact is no doubt due to secondary infection from micro-organisms in the mouth.

The labial chancre seldom becomes phagedenic.

Lingual Chancre.—Chancre of the tongue is the most common of the buccal chancres, next to labial chancre. It is nearly always single, and is usually situated on the anterior third of the dorsal surface. Its most common form is that of an *erosion*, but it may be ulcerated, fissured, or sclerous. The last variety occurs at the tip of the tongue, and may simulate tertiary glossitis (Chapter VII).

Diagnosis.—This is sometimes easy and sometimes difficult. Lingual chancre has been mistaken for *epithelioma*, and excision of the tongue has been performed in such cases. The differential diagnosis is the same as that given for chancre of the lip.

Dental ulcers may become indurated and simulate chancre of the tongue, but they are usually situated on the side of the tongue opposite a broken tooth; also, the submaxillary glands are seldom affected by dental ulcer, while in chancre they are constantly enlarged.

Tuberculous ulcer, especially when it has been artificially indurated by cauterization or by the presence of a broken tooth, etc., and when it has affected the glands, may be easily mistaken for the ulcerated form of lingual chancre. The chief points of difference are shown in the following table:

Tuberculous Ulcer.	Ulcerated Lingual Chancre.
1. Antecedents or actual signs of pulmonary, cutaneous, glandular, or osseous, etc., tuberculosis.	
2. Sometimes situated on lower surface of tongue.	Rarely situated on lower surface of tongue; usually on dorsum.
3. Sometimes multiple.	Nearly always single.
4. Ulceration sometimes extends deeply to muscular tissue.	Ulceration never extends beyond mucosa.
5. Irregular or sinuous outline.	Round or oval.
6. Borders cut out and sometimes detached.	Borders never cut out or detached.
7. Base irregular and yellowish.	Base uniform, smooth, and red or gray.
8. Base usually soft.	Base indurated.
9. Painful on contact.	Not painful.
10. Sometimes yellow tubercle nodules present.	
11. Inoculation in the guinea-pig causes tuberculosis.	

Tonsillar Chancre.—Chancre of the tonsil was first described by Diday in 1861. It is probably more common than is generally supposed, and may easily escape diagnosis. It gives rise to a variable amount of pain and dysphagia.

Tonsillar chancre may occur in three different forms: (1) Erosive, (2) ulcerative, (3) anginal. The *erosive* chancre forms a superficial erosion on the tonsil, varying in size from a lentil to an almond, of a gray or red colour; or sometimes red in some parts and gray in others. Induration of the base is generally present, but difficult to palpate.

The *ulcerative* chancre forms a gray or yellowish-gray ulcer in the substance of the tonsil, the size of the end of the finger. It is accompanied by more pain on deglutition than the erosive form; there is also more induration.

The *anginal* form is less common than the others, but is insidious in nature, and liable to lead to errors in diagnosis. It is complicated by redness and swelling of the tonsil, and accompanied by functional symptoms resembling quinsy. The chancre itself is erosive or ulcerative, and is generally more or less hidden by inflammatory exudation. In other words, this is an inflammatory chancre masked by secondary tonsillitis.

Tonsillar chancre is sometimes complicated by a pseudo-membranous exudation, and occasionally by gangrene.

Diagnosis.—The four main points which differentiate tonsillar chancre from other affections of the throat are—(1) the *unilateral* limitation; (2) the *induration;* (3) the *persistence* for several weeks; (4) the *adenopathy.* The latter is characteristic, and affects the cervical glands under the sterno-mastoid muscle. The satellite bubo is situated at about the middle of the muscle, and sometimes forms a swelling which is easily visible, and painful to touch. This gland may remain enlarged for several months, and is useful in retrospective diagnosis.

Buccal chancres may also occur on the gums, palate, and pharynx, but are rare in these situations. Fournier has only observed one case of chancre on the posterior wall of the pharynx, and this was probably caused by an operation for adenoids, by instrumental or digital contamination.

Treatment.—Local treatment consists in chlorate of potash gargles and mouth-washes, and the application of tincture of iodine, if the chancre is ulcerated.

Nasal Chancre.—Chancres of the nostrils and nasal fossæ are rare. Contagion may be direct, by kissing or by vulvo-facial contact; or indirect, by means of the fingers, instruments, pen-holders, etc. An epidemic of syphilis was caused in Paris some years ago by catheterization of the Eustachian tube by contaminated catheters.

The nasal chancre may be erosive, papulo-hypertrophic, or subulcerative. The latter form may easily be mistaken for eczema or impetigo. J. D. Rolleston has recently reported a case of intranasal chancre in a man of twenty-eight, which was

mistaken for diphtheria, and sent to one of the London fever hospitals.

'On admission, the lower two-thirds of the organ presented a most unsightly appearance, being considerably swollen and of a dusky-red colour. The right ala nasi, which was thickened and very tender, was lined on its inner surface by a membranous deposit, from which on pressure a sanious discharge exuded. There was no excoriation of the philtrum, such as is usually present in severe cases of nasal diphtheria. The left submaxillary and sterno-mastoid glands were considerably swollen and slightly tender. The buccal mucosa and fauces were normal. On the chest and abdomen a polymorphic eruption was present, which, from the absence of pruritus, had hitherto escaped attention. The temperature on admission was 99·2° F., but became normal the same evening, and remained so till his discharge. A smear preparation and three successive cultures of the nasal membrane showed no diphtheria bacilli. A similar examination of the throat was also negative. Though no history of direct or mediate exposure to venereal infection could be obtained, the adenopathy and polymorphic eruption suggested the diagnosis of intranasal chancre. Mercury with chalk (2 grains three times a day) was therefore administered, and the nostril was swabbed with black-wash. The beneficial effects soon became apparent. The voice, hitherto nasal, soon became clear. The deposit within the nostril now consisted of dried-up crusts, which gradually separated, revealing beneath a slightly-raised granular swelling, which resembled in its appearance and induration the primary lesion found in more usual situations. In the course of the next ten days the outer surface of the nose gradually regained its normal appearance, and the intranasal swelling diminished in size.'

Ocular Chancre.—Chancre of the eye was first described by Ricord in 1850. It may be palpebral or conjunctival, and may occur at any age. Contagion may be direct, by kissing, or by licking the eye for the extraction of foreign bodies; or indirect, by the fingers, by spitting, or by contaminated towels, linen, etc. Contagion by spitting and coughing is especially liable to occur in medical men during the examination of throats affected with secondary syphilis. The best safeguard against such contagion is to immediately bathe the eye with 1 in 1,000 perchloride of mercury lotion.

Chancre of the *ciliary border* appears in the form of a hard swelling the size of half a nut. The surface is smooth and red, and sometimes covered by a yellowish-brown scab.

Chancre of the *conjunctiva* is usually situated at the inner angle of the eyelids, and resembles chancre of the ciliary border. When situated at the outer angle, it is divided into two segments, united at the commissure, but partly separated by an ulcerated fissure. This form, like all palpebral chancres, is always much indurated, and may simulate an epithelioma.

Conjunctival chancre is more often situated on the palpebral than on the ocular conjunctiva, and generally causes eversion of the eyelid. Its size varies from that of a lentil to that of an almond; it is round or oval, erosive or subulcerative, with a red or yellowish-red base. It is usually accompanied by more or less conjunctivitis and chemosis.

Adenopathy. — When the chancre is situated at the outer angle of the eye the preauricular gland is enlarged; when situated at the inner angle, the submaxillary glands. In some cases the lower cervical glands are affected down to the level of the clavicle.

Treatment.—The chancre may be bathed with boracic lotion, but no irritating powders or ointments should be applied, and any form of cauterization is contra-indicated.

Facial Chancre. — Chancres on the face may be derived from direct contagion by kissing or by genito-facial contact; indirectly by spitting in the face, or through the medium of contaminated towels, etc., or shaving utensils. It is surprising that the last mode of contagion is not more frequent, considering that patients who are suffering from syphilis do not often give up their habit of visiting the barber, and the latter, as a rule, does not take the trouble to sterilize his razors and shaving-brushes.

It is interesting to note that the facial chancre is the most common of all extragenital chancres *in infancy*. This is explained by the excessive and indiscriminate kissing and fondling to which the unfortunate infants are subject.

Facial chancres are usually single, but sometimes multiple, especially on the chin (probably from infection of several places by an infected razor or shaving-brush). Jullien reports an extraordinary case in which a man contracted three chancres *at the same* time, one on the penis and two on the nose!

Diagnosis.—Facial chancres may be erosive or ulcerative, but sometimes assume a hypertrophic or tuberous form which may simulate epithelioma. They may usually be recognised by the following distinctive points: (1) The circumscribed nature of the lesion, situated in healthy tissues; (2) the induration; (3) the adenopathy; (4) the rapid evolution, as compared with lupus and epithelioma; (5) the smooth, dark red, and often varnished surface. However, in its benign forms the chancre may be mistaken for a patch of eczema, herpes, or impetigo; and when situated on the end of the nose it has been mistaken for a chilblain.

The hypertrophic form may be confounded with tertiary tuberculo-crustate syphilides, and with *epithelioma*. Several cases have been recorded in which chancres of the face have been excised for epithelioma (Fournier, Anderson). However, apart from the objective differences, the much more rapid evolution of the chancre and the much earlier affection of the glands should render such errors avoidable.

Sometimes *sycosis*, either simple or parasitic, may form ulcerated nodules on the face which may simulate hypertrophic chancres; but the sycosic nodule is always inflammatory, and discharges pus by several orifices; the hairs are loose, and in parasitic sycosis the trichophyton is found by microscopic examination.

Mammary Chancre.—Chancre of the breast occurs much more often in women than in men, and is usually due to contagion from a heredo-syphilitic suckling with mucous patches in the mouth. Sometimes it is contracted from the mouth of an adult, either by kissing or biting, or by the practice of 'drawing the nipples' and disgorging the breasts when over-distended with milk.

The chancre is usually situated in the furrow which separates the nipple from the areola; sometimes on the nipple, or on the breast itself. It is usually of the erosive type, but sometimes subulcerative and covered with a brown scab; induration of the base is very marked and lamellar in form.

The *adenopathy* affects the glands in the thoracic wall of the axilla. Sometimes the chancre extends round the base of the

nipple in a semilunar form, and may then be mistaken for simple fissure or 'cracked nipple.'

Mammary chancre is usually single, but sometimes multiple. In one of Fournier's cases there were twenty-three chancres, seven on the left breast and sixteen on the right.

Diagnosis.—Chancre of the breast may be confounded with eczema, Paget's disease of the nipple, ulcerated gumma, or epithelioma, but such errors may usually be avoided by careful examination. The chief point in the diagnosis of extra-genital chancres is to bear in mind that they may occur on any part of the body; if they are not thought of they will escape diagnosis.

From *epithelioma* mammary chancre differs here, as elsewhere, in its more rapid evolution and early affection of the glands. The chancre makes about as much progress in a day as epithelioma does in a month.

From *fissure of the nipple* the diagnosis is not so easy, especially in the semilunar form of chancre. The fissure, however, is smaller and narrower, less indurated, bleeds more easily, is more painful, and does not affect the axillary glands.

Digital Chancre.—Chancres of the finger are probably more common than they appear in the statistics, owing to the fact that many of them are not diagnosed as such. In Fournier's statistics of forty-nine chancres of the hand, thirty were due to *professional contamination* among medical men and midwives, infected during the examination of patients with contagious syphilitic lesions, or by operations on syphilitic subjects whose blood was in an infectious state. Chancres of the hand or finger may also be caused by biting, etc. Hutchinson relates the case of a policeman who contracted a chancre of the knuckle after hitting a man in the mouth, which was affected with buccal syphilides. The handling of dirty linen soiled with the discharges from syphilitic sores is another source of contagion.

The most common situation for digital chancres is *around the nail*, in which region the virus has an easy part of entry. Chancres occurring in other parts of the fingers or hand are usually preceded by some breach of surface, such as a cut, abrasion, chap, chilblain, patch of eczema, etc. Three digits

are affected more often than the others—viz., the index, middle finger, and thumb, in order of frequency.

Varieties of Digital Chancre.—The chancre usually assumes the common *erosive* or the *ulcerative* type. In the latter case it is extensive, with an irregular base, inflamed and diphtheroid in places, owing to secondary irritation. In either case it differs from the usual type of chancre in three points—(1) its configuration; (2) its induration; (3) its painfulness.

When the chancre is situated round the nail, its most common situation, it is *semilunar* in shape. The *induration* is more extensive and spreads into the surrounding tissues, forming a hard mass in which the individual elements are fused together, so that the induration of the chancre cannot be separated from the other tissues. This induration *en masse* is common to all forms of dactylitis, and for this reason digital chancre is often mistaken for a whitlow. Chancres of the terminal phalanx of the finger are often extremely *painful*, especially when they extend under the nail.

Chancre-panaris.—The most important type of digital chancre is that called by Fournier the chancre-panaris, which closely resembles whitlow. In this form the terminal phalanx of the finger is red, swollen, and bulbous, painful and sensitive to touch, and indurated *en masse*. The swelling of the tissues extends to the second phalanx. The surface of the chancre forms an irregular ulcer with ragged edges and a grayish red, sanious, and sometimes diphtheroid base. In fact, the whole aspect is that of whitlow rather than syphilitic chancre. This form of chancre is also remarkable for its slow evolution and long duration, which may extend over several months. The nail often becomes separated by ulceration, and in some cases necrosis of the bone may take place.

Occasionally the digital chancre assumes the *hypertrophic* or tuberous form, and may be mistaken for epithelioma. A *fungating* form has also been described, but this is rare.

Adenopathy.—The glands affected are the epitrochlear and the axillary. They are usually hard like other satellite buboes, but may suppurate in cases where the chancre becomes much irritated and inflamed.

Treatment.—Local dressings of calomel cream are useful, and boracic acid fomentations if there is much pain or inflammation. Iodoform ointment is perhaps the best local application, if the patient has no objection to its odour.

Anal Chancre.—The frequency of chancres of the anus varies in different countries, being greater in those where sodomy is prevalent. Thus, out of a total of forty-two extra-genital chancres observed by During at Constantinople, thirty-one were situated in or near the anus or in the rectum; and out of these thirty-one chancres, twenty-six occurred in children and four in men!

The principal causes of anal chancre are the practice of sodomy, criminal assaults on children, buccal contagion, contamination by infected fingers, instruments, linen, enema syringes, etc.

Anal chancre may be concealed within the anal orifice, and can then only be seen by stretching the anus, either by the fingers or by a rectal speculum. It then appears as a deep red oval or elliptical erosion or subulceration with a smooth base. On removal of the speculum it shrivels up, and becomes folded on itself. It causes some pain on defæcation, but much less than that caused by anal fissure. Induration is seldom perceptible. Owing to its situation it is liable to irritation and inflammation.

Diagnosis.—The chief lesions which may be confounded with anal chancre are—(1) ulcerated hæmorrhoid; (2) anal fissure; (3) tuberculous ulcer. In the case of *ulcerated hæmorrhoid* there will be a previous history of piles and bleeding, and a violent attack of piles, accompanied by strangulation and gangrene, preceding the ulceration. Moreover, a group of external piles is usually visible.

Anal fissure forms a smaller and narrower lesion than chancre. It is more painful, and is not accompanied by the inguinal adenopathy of anal chancre.

Tuberculous ulcer is not uncommon in the anal and perianal region, but can only be confounded with chancre in its early stages. Even then it differs from chancre in its distinct borders, which are often detached, in its depressed base, in its

yellowish colour, in the absence of induration and inguinal adenopathy, and in its more chronic evolution.

An important point in the diagnosis of anal chancre is the presence of the *satellite bubo*, which can usually be felt as a hard lump in the *outer third of the groin*.

Treatment.—The best local applications for anal chancres are calomel and iodoform ointments.

Vaccinal Chancre.—Vaccinal chancre is caused by vaccination with lymph which has been accidentally mixed with syphilitic virus. It does not differ objectively from any other cutaneous chancre.

It may appear before or after the fall of the scabs of the vaccinal pustules, and in the former case is masked for a time. Vaccinal chancre always appears later than the vesicles of vaccinia, since the minimum incubation period of syphilitic chancre (fifteen days) is considerably longer than that of vaccinia.

The chancre may also appear at points of vaccination which have not 'taken.'

Diagnosis.—When the chancre develops under the scabs of the vaccinal pustules, it is impossible to diagnose at once. The chancre is then invisible, and the only sign is persistence of the scabs longer than usual. It is only after one or two weeks that a vaccinal chancre is suspected, by the appearance of a new lesion after the scabs have fallen, or by the presence of hard glands in the axilla.

Sometimes *ulcerated vaccinal pustules* may be mistaken for syphilitic chancre, but differ in the following points: (1) They appear from the twelfth to the fifteenth day, while chancre usually appears after the third week, never before the fifteenth day; (2) they generally affect all the pustules, while chancre only develops on one or two; (3) the lesion is an acute suppurating ulcer with an inflammatory areola, and œdema or pseudo-erysipelas of the surrounding tissues; (4) absence of the special characters of chancre, with its induration and satellite bubo.

Source of Contagion.—Since the substitution of calf lymph for human lymph the epidemics of vaccinal syphilis which formerly occurred are seldom seen nowadays. However, it

is necessary to bear in mind that contagion may be conveyed by contaminated lancets and needles. In vaccinating batches of infants it is therefore important to pass the lancet or needle through a flame after each operation, for any one of these infants may be in a latent state of hereditary syphilis.

Chancres of the Trunk and Limbs.—These may occur on any point of the body which happens to be inoculated by direct or indirect contagion. Direct contagion may take place at the umbilicus, in the axilla or ham, etc., from abnormal sexual connection or by kissing. Indirect contagion may occur from contaminated linen, towels, bedclothes, etc. There are certain sources of contagion which merit special mention.

1. *The nitrate of silver crayon*, according to Fournier, is a more common source of contagion than is generally believed. In this case the contagious matter is probably conveyed by the holder, and not by the crayon itself, which would probably destroy the vitality of the virus.

2. *Tattooing* has often been known to convey syphilitic contagion, either by the contaminated saliva of the operator being used to mix the colours, or by using instruments which have previously been used on a syphilitic subject.

3. *The cupping glass* has also been the origin of syphilitic infection, and Duncan Bulkley has collected the accounts of thirteen epidemics of syphilis which were produced in this way, chiefly in former times when cupping was performed by barbers and other unqualified persons.

4. *Skin-grafting* is another possible source of syphilitic contagion.

5. *Latrines* may convey syphilitic infection indirectly; but gonorrhœa is much more likely to be contracted in this way than syphilis.

Prognosis of Extragenital Syphilis.—There is a prevalent idea that extragenital chancres are usually followed by severe forms of syphilis. However, according to Fournier, the fact of the extragenital situation of the chancre does not in itself render the prognosis grave.

The fact that these chancres are often followed by severe syphilis is due rather to circumstances connected with the

patient. For instance, digital chancre contracted by a medical man may be followed by severe syphilis, because medical men are notoriously bad subjects for syphilis, owing to the mental depression caused by the knowledge of their disease, and to their liability to neglect treatment owing to stress of work. As Ricord remarked: 'One of the worst conditions for contracting syphilis is to be a doctor.'

Again, chancres of the face, or mammary chancre in a woman, may cause much mental distress and depression, and these are bad factors in the prognosis of syphilis. We may therefore conclude that if extragenital chancres are followed by severe forms of syphilis this is mainly due to secondary causes.

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CHAPTER V

SYPHILIDES

SYPHILIS affects the skin and mucous membranes, both in the secondary and tertiary stages, in the form of diverse eruptions called *cutaneous* or *mucous syphilides.*

Like all the manifestations of syphilis, the syphilides originate in changes in the small bloodvessels (Endo-periarteritis, Chapter VI) which give rise to perivascular cell infiltration of various degrees. According to the degree of this perivascular infiltration, the syphilide manifests itself in the form of erythema, papule, or gumma, the pathological process being essentially the same in all cases. In erythema the changes in the vessels are slight, and consist only in hyperæmia with slight infiltration of round cells; a further degree of cell infiltration into the papillæ of the skin gives rise to the papular syphilide; a still greater accumulation of cells with more pronounced endo-periarteritis causes the formation of tubercular syphilides and cutaneous or subcutaneous gummata. Secondary changes in the epidermis form varieties in the papular syphilide—such as papulo-squamous, papulo-vesicular, papulo-erosive, or papulo-ulcerative. The gummatous syphilides are liable to caseate and ulcerate, forming ulcerative syphilides or ulcerative cutaneous gummata.

Bacteriology.—Syphilides appear to be due to limited colonies of the microbic agent, for they are very contagious when they become exudative from loss of the epidermic covering. Recently the *Spirochæta pallida* has been found in secondary cutaneous syphilides and mucous patches, but rarely in tertiary syphilides. It has also been found in the fluid of blisters applied to the skin of syphilitic infants, and is

therefore probably present in the skin before visible syphilides appear (Levaditi).

General Characters of Syphilides. — Syphilides vary very much in form, and may reproduce almost all the elementary types of dermatoses. They are characterized (1) by the absence of fever and inflammatory symptoms; (2) by polymorphism, more than one type of dermatosis being usually present; (3) by the tendency to form circles or segments of circles; (4) by their symmetrical distribution in secondary, but not in tertiary, syphilis; (5) by the usual absence of pruritus (a certain amount of itching may, however, be present in syphilides affecting hairy regions and opposed surfaces, such as the axillæ, groins, scrotum, etc., also in alcoholic or neurotic subjects); (6) by the tendency of the elements of the eruption to assume a smoked ham or, more rarely, copper colour. This colour is due to the deposit of blood-pigment disseminated in the cellular infiltrations, and the pigmentation lasts for some time after the eruption has subsided.

Syphilides may appear on any part of the skin, but have a predilection for certain parts, such as the palms and soles, the forehead, neck, and opposed surfaces. Secondary syphilides affect the flexor surfaces of the limbs more commonly than the extensor surfaces, and are rare on the backs of the hands and feet.

Accessory Causes.—Certain causes influence the intensity of syphilitic eruptions. The chief of these are—(1) the quality of the virus; (2) the nature of the soil (a tuberculous or alcoholic subject is liable to severe syphilitic eruptions, and in alcoholic subjects syphilides are often profuse and confluent, and sometimes of a bright red colour); (3) local causes, such as bad circulation and the presence of other microbes in the skin.

Local irritation favours the development of syphilides in certain situations; for instance, laryngitis in singers, mucous patches in smokers; palmar syphilides, eruptions of the genital organs and anus, etc. Sometimes cutaneous papules may become indurated, when they are subject to irritation and neglect, and resemble chancres. Certain affections of the

skin may also act as irritating causes and provoke syphilitic eruptions; for instance, seborrhœa of the scalp or face, eczema, varix, blistering applications, etc. Lang and Schiff have described iodic eruptions which developed into syphilitic ulcerations. The presence of numerous microbes on the surface of the skin is a cause of irritation which may excite the syphilitic process, and also cause secondary infection of the lesions (ecthyma).

Evolution. — Secondary syphilides are superficial, and undergo resolution without leaving cicatrices. Resolution commences in the centre of the elements, and varies according to the date of the disease and according to the presence or absence of aggravating causes, such as those mentioned above. Tertiary syphilides, on the other hand, affect the tissues more profoundly, causing necrosis of the tissue elements and consequent scarring.

The earlier secondary eruptions are disseminated; later on there is a tendency to become more localized in groups, more or less symmetrically, according as the disease advances in age. In tertiary syphilis the elements of the eruption become larger, fewer in number, and show a tendency to arrange themselves in the form of circles or parts of circles. In a general way, syphilitic eruptions tend to progress eccentrically, both as regards the whole eruption and the elements which constitute it. Although polymorphism is the rule in secondary eruptions, these are often of a single type, or monomorphous, and may preserve their individuality throughout their evolution. Eruptions of quite different types may thus succeed each other in the same individual.

In some persons the eruptions are exclusively cutaneous, chiefly consisting in dry papular or squamous syphilides, without the mucous membranes being affected. In others, a series of outbreaks affects the mucous membranes and certain parts of the skin, such as the scrotum, occurring every time in the same situations. Recurrence *in situ* may be with elements of the same or of a different type. Balzer has observed papular syphilides develop on the cicatrices of ulcerative syphilides.

Syphilitic eruptions have been noticed to temporarily dis-

appear during an attack of pneumonia, erysipelas, or typhoid fever. Gaucher has described cases of zoniform syphilides following the course of a nerve; others have reported syphilides as avoiding the paralyzed limbs in paralytic subjects affected with secondary syphilis. Hence the integrity of the nervous system appears to play some part in the development of syphilides.

Purpuric eruptions are rare in cutaneous syphilis, and are possibly due to secondary causes; a purpuric roseola, however, is sometimes observed.

Late Secondary Syphilides.—Fournier draws attention to the fact that syphilitic manifestations having the characters of the secondary period may occur in what is usually regarded as the tertiary period—viz., as late as ten or even twenty years after the chancre. The most important of these late secondary syphilides are palmar and plantar syphilides, recurrent roseola, tertiary erythema, mucous syphilides of the mouth and genital organs, and depapillating glossitis.

These late syphilides are characterized (1) by reacting to mercury rather than to iodide; (2) by their frequent recurrences; (3) by their contagiousness. They often occur in association with gummatous or other tertiary manifestations. Fournier has collected 1,096 cases of secondary syphilis occurring after the third year, including nine cases of palmar syphilides which appeared upwards of twenty years after the chancre. He attributes these cases to attenuation, but not extinction, of the virus by an insufficient mercurial treatment.

The importance of these cases lies in the fact of their *contagiousness*, which shows that syphilis may be contagious in some cases long after the third year. It is therefore difficult to fix the period at which syphilis ceases to be contagious, except by the presence or absence of the *Spirochæta pallida*, if this be the true pathogenic microbe of syphilis.

Classification of Syphilides.

The classification of syphilides has been unnecessarily complicated and confused by attempts to classify the cutaneous manifestations of syphilis according to the cumbersome nomen-

clature of the dermatologists. It must be borne in mind that any classification of syphilides is more or less artificial, although useful for clinical purposes. All syphilides, as previously pointed out, are only different degrees of the same pathological process, and several different forms are often present at the same time.

The following table, modified from Balzer and Fournier, is sufficient for all practical purposes:

ERYTHEMATOUS SYPHILIDES.

Roseola. Recurrent roseola. Tertiary erythema.
Pigmentary syphilide or melanoderma syphiliticum.

PAPULAR SYPHILIDES.

Simple papular syphilides: Lenticular; lichenoid; corymbose; circinate; in rosettes (*en cocarde*), in placards (*en nappe*); papulo-atrophic.

Papulo-squamous syphilides: Pityriasiform; psoriasiform; eczematiform.

Papulo-erosive or exudative syphilides: Simple papulo-erosive; mucous patch; condyloma.

Papulo-vesicular syphilides: Papulo-crustate; miliary or herpetiform; acneiform; varioliform.

Papulo-pustular syphilides: Impetiginous; ecthymatous rupia.

Papulo-ulcerative syphilide.

Papulo-bullous syphilide (pemphigoid of infants).

GUMMATOUS SYPHILIDES.*

SUBCUTANEOUS GUMMATA.

Erythematous Syphilides.

Roseola. — This is nearly always the first eruption of secondary syphilis, and marks the commencement of the

* The French writers use the term 'tubercular' syphilide for 'gummatous,' but this term is best avoided, owing to confusion with tuberculosis. Professor Fournier some time ago suggested the term 'taberous' instead of 'tubercular,' but this term has not come into general usage.

secondary period. It usually appears in the seventh week after the commencement of the chancre, or about the forty-fifth day. In some cases it may appear earlier, and has been noted as early as the twentieth day; at other times it may be delayed, especially after mercurial treatment administered during the period of the chancre.

The eruption first appears on the flanks, abdomen, and chest, less commonly on the limbs, and rarely on the face. It consists of irregular rose-red spots, more or less discrete or confluent, sometimes limited to a diffuse mottling of the skin. It is rendered more apparent in the early stages by being viewed through cobalt glass. Later on the spots become darker in colour, reddish-yellow, and sometimes purpuric. In typical cases the spots are not raised above the skin, but in some cases, known as *urticarial roseola*, they have more or less of a nettle-rash appearance. Some cases are *scarlatiniform*. The rash causes no itching, and is often not noticed by the patient.

The duration of the roseola is very variable; it may be transient, only lasting a few days, or it may last for several weeks in spite of treatment. Sometimes the appearance of the roseola is delayed till after the sixth month.

Recurrent Roseola.—Under this term are included cases of roseola which recur several times during the course of the disease. They are generally formed by a more discrete eruption, consisting of fewer, paler, and larger spots, often arranged in a circinate manner. Fournier says these cases only occur after mercurial treatment. They include what has been called *tertiary erythema*, which is regarded by Unna as a 'neurosyphilide,' caused by the action of the syphilitic toxin on the vaso-motor nerves. The eruption occurs on the trunk, and may coincide with ulcers of the limbs.

Although roseola is apparently only a hyperæmia, microscopical examination has shown the presence of vascular changes affecting the endothelium of the small vessels, and infiltration of the dermis with plasma cells. In other words, the condition represents the first stage of the perivascular cell infiltration and endarteritis which constitutes the fundamental pathology of all syphilitic lesions.

Diagnosis. — The diagnosis of syphilitic roseola is usually easy, as there are generally the signs of chancre and its satellite glands remaining. Syphilitic differs from *simple roseola* in the absence of febrile symptoms and itching; simple roseola is 'seasonal,' and usually attacks the face. A *copaiba rash* is sometimes mistaken for roseola, but the spots are redder, more discrete, and situated especially on the limbs, about the joints, and on the back of the hands. Syphilitic roseola is occasionally *scarlatiniform* in character, and must be diagnosed from scarlet fever by the general symptoms.

Pityriasis versicolor presents no difficulty in diagnosis, as the eruption is on the surface of the skin and not in its substance. Moreover, scales can be scraped off and examined under the microscope for the fungus (*Microsporon furfur*). It is generally of a yellower colour than syphilitic roseola.

Pityriasis rosea is often mistaken for roseola. The spots, however, differ in the presence of desquamation, which covers them in a few days with a fine floury powder. The syphilitic roseola never desquamates. In pityriasis rosea the so-called 'herald' or primary patch may be found, of an oval shape and bistre colour, with a slightly raised red border.

Antipyrin sometimes causes an eruption of disseminated confluent red patches, but the invasion is more sudden and the evolution more rapid than in the case of syphilitic roseola.

Erythema multiforme is more discrete and more purple in colour than syphilitic roseola. It chiefly affects the wrists and ankles, which are seldom affected by roseola.

The syphilitic roseola must not be mistaken for the marbled appearance of the skin which is sometimes seen after undressing a patient in a cold room. In this condition there is a livid reticulum enclosing areas of normally-coloured skin, while in the syphilitic roseola the erythematous spots occur as islands in a reticulum of normal skin. In other words, the one is a negative and the other a positive picture.

Pigmentary Syphilide. — This is a peculiar pigmentary condition affecting chiefly the sides and back of the neck. It is apparently more common in women, but this may be because the skin of the neck is generally whiter than in males.

The pigmented area is of a grayish bistre colour, and forms a reticulum enclosing islets of normal skin, which appear whiter by contrast. This condition persists for a long time, and does not react to treatment. It has been facetiously termed the 'collar of Venus.' Although this condition is most usually found on the neck, it also occurs in the axilla, on the thighs and on the trunk. Balzer mentions a case occurring on the scalp in a bald person. It is very rare on the face.

The exact nature of the pigmentary syphilide has been the subject of much discussion. Fournier regards it as a primary pigmentation of a parasyphilitic nature, and not a secondary condition. Balzer and others consider that it is produced by a peculiar evolution of the eruptive elements of the secondary period, roseola or papules, and that these elements, which are sometimes recognisable at its first appearance, are necessary for the development of the pigmentary syphilide, or *melanoderma syphiliticum*.

According to this view, an extra quantity of pigment is produced, which extends beyond the limits of the eruptive elements; the latter become decolourized in the centre by absorption of the pigment, but this persists at the periphery and forms the meshes of the pigmentary reticulum. Moreover, the pigmentation may affect the deeper parts of the skin, and De Maieff has found obliterating arteritis of the vessels in the deeper layers of the skin in cases of pigmentary syphilides. These vascular lesions may explain extensive pigmentation, by extravasation of blood-pigment accompanying the perivascular infiltration of the tissues of the skin.

Diagnosis.—Although opinions may differ as to the pathology of the pigmentary syphilide, all are agreed as to its value in the diagnosis of syphilis.

In *vitiligo* there is more marked leucodermia, which also affects the hairs, and there is an absence of the melanodermic network of the pigmentary syphilide. *Uterine chloasma* affects the face more than the neck. The pigmentation of *Addison's disease* is diffuse, and also affects the mucous membranes.

Pigmentation often follows many syphilitic eruptions, and even the chancre; but it is more pronounced than that of the

pigmentary syphilide, and is situated either in the same places as the eruptive elements or immediately around them. Pigmentation, however, is not peculiar to syphilitic eruptions, and often follows many chronic dermatoses; for instance, urticaria pigmentosum, chronic eczema, lichen, psoriasis, etc.

Papular Syphilides.

Pathology.—The *papule* is the fundamental type of the syphilides, and is constituted by a circumscribed inflammation of the superficial dermis and papillæ. The vessels are affected with endo-periarteritis, and give origin to a perivascular cell infiltration in the form of nodules. According to the researches of Unna, these nodules are formed by cells which are either migratory or derived from the fixed connective-tissue cells. At a certain distance from the vessel multinuclear giant cells are found, each surrounded by epithelioid cells with clear protoplasm which are not easily stained, and plasmatic cells with granular protoplasm easily stained with methylene blue. This group of cells is called the *plasmoma*. In the substance of the nodules the elastic tissue of the dermis becomes rarefied, and there is a new formation of fibrillar tissue, which surrounds the cells, as in the chancre. The disposition of the cell infiltration round the vessels and the grouping of the cells is practically the same whatever relation the papular focus bears to the pilosebaceous follicles, whether it is a lenticular papule, a miliary papule surrounding the pilosebaceous follicle, or large papules in sheets. In the latter the nodules are more diffuse and composed of less compact plasmomata than in the case of the lenticular papule. Giant cells are especially found in acneiform and lichenoid syphilides. Obliteration of the vessels occurs in tertiary syphilides, but is rare in secondary syphilides. The lymphatic vessels are dilated. To these fundamental changes in the dermis are added secondary and variable lesions of the epidermis. Owing to a certain degree of œdema, the intercellular spaces of the epithelium become dilated, the eleidine diminishes, and desquamation occurs. In large exudative papules, or *condylomata*, there is not only œdema, but also

migration of leucocytes through the epidermis. The latter becomes proliferated unequally, and sends deep prolongations between the elongated papillæ. If the papule is situated in a fold of the skin, in a moist region, it becomes exudative, and the exudation dries up, forming more or less adherent crusts, in which pyogenic organisms are found. When the epidermis resists, the horny layer may undergo considerable hypertrophy. The exuded liquid may accumulate in the intercellular spaces and in the cavities formed by destruction of the cells of the Malpighian layer, giving rise to *vesicles* and *pustules*. Hence the numerous clinical varieties of syphilides, the fundamental anatomical character of which is always papular infiltration of the dermis. In most cases the cellular infiltration of the papule takes place in the papillæ of the corium—*i.e.*, in the most superficial part of the dermis. More rarely the infiltration is in the deeper layers of the dermis, and causes no visible change on the surface. This variety of *intradermic papule* occurs especially in the pigmentary syphilide, and in the case of eruption followed by *atrophic papules*. Finally, the papular infiltration may occur under the dermis, forming nodosities which may be felt under the skin. Examination of these subdermic nodosities has shown that they have the same structure as papules, and that they develop round the small veins of the hypodermis. They are therefore due to nodular thrombo-phlebitis. *Ulcerative papular syphilides* depend on the intensity of the exudative inflammation, which ends in softening and suppuration. The pus cells accumulate in the cavities of the epidermis and in the superficial part of the dermis (*papulo-pustular syphilide*); the epidermis ruptures, and the *papulo-ulcerative syphilide* is formed. Pyogenic microbes nearly always take part in this acute inflammatory process, and it is to these that the peripheral extension of the ulcers is due, which constitutes the forms known as syphilitic *ecthyma* and *rupia*. In the latter the pus dries in superposed crusts, which extend in proportion to the increase of the ulceration. In the *serpiginous tertiary syphilide* the ulcerative process is confined to the periphery of the lesion, while healing takes place in the centre. This causes

the annular or serpiginous form of the lesions. Ulcerative syphilides leave cicatrices varying with the extent of the ulcerative process, and these cicatrices are usually deeply pigmented. The process is essentially a mixed one, in which the syphilitic process is associated with pyogenic organisms (Balzer).

Papular Syphilides.—Papular eruptions may accompany the roseola, or even in some cases precede it; but, as a rule, they appear after the roseola, generally during the third month. The early papular eruptions have a tendency to generalization, but have a predilection for certain parts, such as the flexor surfaces of the limbs and the forehead. Papular syphilides have received different names according to their size and arrangement, the chief varieties being the lenticular, large papular, miliary or lichenoid, corymbose, circinate, and syphilides in the form of rosettes (*en cocarde*), in sheets or placards (*en nappe*), or in the form of bouquets.

Lenticular Syphilide.—This is the type of the papular eruptions. The elements consist of smooth, rounded, slightly raised ham-coloured papules, somewhat resembling lentils set in the skin. Sometimes they are surrounded by a ring of fine desquamation, known as the collarette of Biett. The lenticular syphilide occurs on the trunk, limbs, face, scalp, forehead, and around the mouth. It persists for months if left alone, but generally disappears under mercurial treatment. It has a tendency to recur in a less diffuse but more circinate form, especially round the mouth. Lenticular elements occur in polymorphous syphilitic eruptions, but they may constitute a persistent type which is often resistant to treatment. It is the intradermic form of lenticular syphilide which forms the *atrophic papular syphilide*, by destruction of the elastic tissue of the dermis, causing depressions simulating lineæ albicantes (Balzer).

The *corona veneris*, which is characteristic of secondary syphilis, is formed usually by lenticular syphilides at the junction of the forehead with the scalp. It differs from the 'corona seborrhœia,' due to fatty pityriasis, by not extending on to the scalp.

Small Papular or Lichenoid Syphilide.—This is formed by small papules the size of a pin's head, more convex and more confluent than those of the lenticular eruption. The papules may occupy the summit of the papillæ or the base of the hairs, and often coincide with keratosis pilaris. They are often grouped in rings or semicircles. The eruption occurs on the trunk and limbs, the naso-labial furrow, the chin, and the forehead, at the root of the hairs (one form of the 'corona veneris'). In these situations on the face they present a seborrhœic aspect.

The lichenoid syphilide is often persistent and rebellious to treatment. The epidermis is thickened on the surface of the papillæ or in the hairy follicles, and in the dermis there is perivascular cell-infiltration around the vessels of the follicles and sudoriferous glands.

Fournier describes a variety of small papular syphilide which he calls the *punctate papular syphilide*. This occurs on the trunk and limbs, but not on the face. It is characterized by the smallness of its elements, and by their extreme confluence.

Diagnosis.—The lichenoid syphilide differs from *lichen planus* in the following points:

Lichen Planus.	Lichenoid Syphilide.
1. Papules smooth, shiny, flat, and arranged in a mosaic of polygonal facetes.	Papules granular, convex, and circular, like millet seeds. Sometimes squamous or crowned with a small crust. Harder than lichen papules.
2. Papules lose their individuality by being grouped in placards.	Papules generally preserve their individuality, and have little tendency to be grouped in placards.
3. Terminal pigmentation occurs in successive regions, constituting a polymorphous appearance.	Terminal pigmentation not constant, and when it occurs affects the whole eruption at the same time.
4. Pruriginous.	As a rule non-pruriginous.

Corymbose Syphilide.—This is a form of eruption in which a group of papules surrounds a larger central papule. This

form of syphilide is generally associated with, or secondary to, other types, but may occur independently, especially in late secondary syphilis. The syphilide 'in bouquets' is a variety in which the central papula is absent.

In the later secondary period other varieties of papular syphilides occur: (1) The large *papular syphilide* differs only in the size of the papules, which feel like pieces of cardboard in the skin, and leave brown spots after resolution. They are generally mixed with smaller papules. (2) The late secondary syphilides are often characterized by their *circinate* or *annular* form, sometimes forming concentric circles, and at other times segments of circles and spirals. (3) The *papular syphilide 'en nappe'* forms sheets or placards which sometimes cover most of the vulva and perineum. They are formed by the coalescence of groups of papules. (4) The *papulo-tubercular syphilide* forms the connecting-link between the secondary and tertiary periods. It is constituted by large papules forming more or less extensive placards, and is really a form of gummatous infiltration of the skin, the gumma being, as previously stated, only a further degree of the pathological process which forms the papule. (5) The so-called *syphilide en rosette* is a name given to the variety of coloration caused by the development of papules in the same situation as other papules which are undergoing resolution. (6) The papules, when situated in a fold of flexion, such as the genito-crural, intergluteal, or palpebral folds, may become divided by a fissure, which subsequently ulcerates, forming rhagades. (7) Fournier describes a *verrucose syphilide*, formed by small warty papules, situated especially in the naso-labial furrow, and resembling grains of tapioca. They were regarded by Ricord as characteristic of syphilis.

Papulo-squamous Syphilide.—In this there is desquamation of the epidermic covering of the papule. In the case of the *psoriasiform syphilide* this desquamation takes the form of dry squames, more or less adherent, and simulating those of psoriasis. The psoriasiform syphilide is especially common on the palms and soles, and was formerly known as 'palmar and plantar syphilitic psoriasis.'

Diagnosis.—The chief points of difference between the psoriasiform syphilide and psoriasis are: (1) In the syphilitic lesion the papular infiltration is deeper than in psoriasis; (2) the scales are thinner and less adherent; (3) the colour is darker, and more like that of smoked ham.

In psoriasis, on the other hand, the scales are large, thick, white, and stratified, and leave a white, waxy mark when scratched with the finger-nail; when removed *en masse*, they have blood-points on the denuded surface.

Palmar and Plantar Syphilides.—These are late secondary syphilides, sometimes unilateral, sometimes bilateral, and have a tendency to become chronic. They are most common in the first two or three years of the disease, but often occur much later, and frequently constitute a manifestation of recurrent syphilis. They often assume a circinate form, and are liable to become fissured by irritation, especially in washerwomen and mechanics.

The *plantar syphilide* generally affects the middle of the foot, more rarely the heel and toes.

The *palmar syphilide* is often most difficult to diagnose from *palmar eczema*. The chief points of difference are given in the following table:

Palmar Eczema.	Palmar Syphilide.
1. Nearly always bilateral.	Generally unilateral, but not always.
2. Borders flat and not raised.	Borders often raised, thickened, and formed of exfoliating lamellæ.
3. Base soft and uniform.	Base infiltrated, parchmenty, and irregular.
4. Frequently extends on to sides of hands and sometimes on to dorsum.	Limited exclusively to the palm, extending by serpiginous extension, and accompanied often by small exfoliating satellite lesions.
5. Sometimes affects the whole surface of the palm.	Generally confined to a part of the palm only.
6. Margin of eruption ill-defined and ragged, and interrupted by islets of healthy tissue.	Margin of lesion is red, scaly, and well defined in most places, but irregular, serpiginous, and undermined.
7. Sometimes eczema is present elsewhere.	Therapeutic test.

Sabouraud states that syphilis, psoriasis, and eczema may cause lesions in the palm of the hand which are sometimes impossible to differentiate.

In the earlier stages of secondary syphilis papules may appear in the palm as part of the general papular eruption. Later on the epidermis exfoliates over the situation of each papule, and this condition may not be attributed to its true cause after the general eruption has disappeared. Fournier describes two forms of palmar and plantar syphilides: (1) *Secondary* or late secondary syphilides, occurring either as lenticular, peeling spots, or as irregular patches, sometimes circinate; (2) *tertiary* syphilides, characterized by infiltration of the dermis, parchmenty skin, and lamellar desquamation, sometimes with a raised and thickened border. He states that the late secondary form is contagious, and the tertiary not so.

Certain *pityriasiform* and *eczematiform* syphilides may resemble seborrhœic dermatitis. In these cases the epidermis forms adherent fatty squames, situated on a dark red pigmented base. In these forms there appears to be an eczematous process in the glands of the skin associated with elements of the syphilitic eruption placed around the follicles. This mixture of seborrhœic and syphilitic lesions is observed in syphilides of the border of the scalp (corona Veneris) and on the face and palms of the hands.

Papulo-erosive Syphilides.—This type occurs in parts where the skin is moist—the external genitals, axillæ, groins, and folds of skin generally. Owing to the moisture of the parts, the epidermis covering the papules becomes sodden and exudative, and liable to erosion and secondary ulceration. The hypertrophic papulo-erosive syphilide forms the large flat papules, known as *condylomata lata*, which are common about the genital organs of women.

The papulo-erosive syphilide is the homologue of the *mucous patch*, which is the type of syphilides of the mucous membranes. The discharge from these lesions is extremely contagious, and is responsible for far more contaminations than are caused by chancres. The *Spirochæta pallida* can be found in scrapings from the sores.

The exudation from papulo-erosive syphilides sometimes dries up into yellowish-brown, more or less adherent scabs; at other times a diphtheroid exudation is produced. When situated about the folds of skin—in the axillæ, around the ears, nostrils, or anus, or between the buttocks or fingers—fissures or *rhagades* are formed Ulceration may take place in papulo-erosive syphilides, owing to secondary infection by pyogenic organisms, constituting one form of *papulo-ulcerative syphilide.*

Condyloma Latum.—This form of syphilide is especially common in the region of the vulva in women. It also occurs in men on the scrotum and perineum. Condylomata are flat, sessile, hypertrophic papules of various sizes, grayish-white or pink in colour, and exuding a fœtid discharge. The surface is formed of sodden epidermis, in which the *Spirochæta pallida* can be found. These papules often fuse together to form large placards, which may cover the parts round the vulva and extend on to the groins and thighs. In women who neglect hygienic measures they often form large cauliflower growths with fissures and ulcerations. These differ from gonorrhœal vegetations in not being branched. However, the enormous vegetating masses which are so common in low-class dirty prostitutes are probably a mixture of condylomata and gonorrhœal warts, aggravated by chronic vaginal discharges and want of cleanliness.

On the mucous surface of the vulva the mucous syphilide is seen in the form of erosions and mucous tubercles. In fact, in this region transitional forms can often be seen from the large papular syphilide on the skin of the thigh to the mucous patch inside the labia, various stages of condylomata intervening in the groin and on the cutaneous surface of the labia. The condyloma latum is thus the connecting-link between the large papular syphilide and the *mucous patch* (p. 120).

Condylomata and vulvar mucous patches are very contagious, and are the most common cause of syphilitic contagion.

The vulvar mucous patch differs from *soft chancre* in the absence of the punched-out appearance and irregular yellow

base. Moreover, in soft chancre there is generally a bubo, and the bacillus of Ducrey can be found.

Papulo-vesicular Syphilides.—In this form the papule becomes vesicular, the vesicle ruptures, and the papule is capped by a scab or crust, forming the *papulo-vesiculo-crustate syphilide*. This form is common, and is usually mingled with simple lenticular papules.

Herpetiform or Miliary Syphilide.—Under this term Fournier describes an eruption of numerous vesicles, the size of a pin's head, often confluent, and situated chiefly on the limbs and trunk. The vesicles are ephemeral, and are soon replaced by scabs. This form of syphilide differs from herpes in being irregularly disseminated, instead of forming groups of vesicles.

Acneiform Syphilide.—This is constituted by small dark red, hard papules, with a small vesicle at the summit which dries up into a brown adherent scab. It is especially common on the scalp in early secondary syphilis, and may also occur on the face and thorax. This form of syphilide affects the hair follicles and sebaceous glands, and is hence a *follicular syphilide*. It differs from *acne vulgaris* in the dark red colour of the papules; in their smaller and more uniform size; in the absence of comedones; in being more disseminated, more acute, and more transitory. Acne vulgaris is more polymorphous, and consists usually of larger elements (comedones, pustules, and inflamed nodules), and affects the seborrhœic regions (forehead, nasal furrow, chin, mid-sternal and interscapular regions). Moreover, the acneiform syphilide usually coexists with other papular syphilides.

Varioliform Syphilide.—This is constituted by an eruption of round, flattened papulo-vesicles, affecting the trunk, face, and limbs. The varioliform syphilide is sometimes mistaken for small-pox, especially as it is sometimes accompanied by febrile symptoms. This error, however, should be easily avoided. In typical unmodified small-pox there is sudden onset of fever with severe headache and lumbar pain; the rash appears on the third day in the form of red shotty papules, first appearing on the face, forearms, and wrists, and

afterwards on the trunk and limbs; the rash undergoes a regular evolution, forming vesicles in the course of three or four days and pustules in seven days. The elements of the varioliform syphilide are ham or copper coloured, and do not go through the same cycle of evolution as the small-pox pustules; fever and general symptoms are much less pronounced, and there are usually other syphilides or signs of syphilis present. Cases of modified small-pox occurring in vaccinated persons undergo an abortive evolution, and most of the vesicles dry up without forming pustules. These cases resemble chicken-pox much more than varioliform syphilis. There are thus great differences between the varioliform syphilide and both modified and unmodified small-pox, and hence there is little excuse for sending such cases to small-pox hospitals.

Papulo-pustular Syphilides.—In this case the syphilitic process is complicated by the action of pyogenic organisms, causing the formation of pustules with consequent ulceration, varying in degree. The syphilitic virus must, however, be regarded as the chief agent in the production of these ulcerations, because the pustular element has always a papular base of infiltration which rapidly extends and precedes the ulceration. Moreover, these syphilides often occur in successive outbreaks with the same characters. Lastly, the effect of treatment is too rapid to leave any doubt as to the preponderance of syphilis in their development.

The mildest form of pustular syphilide constitutes the so-called *syphilitic impetigo*. This forms superficial ulcerations covered with brownish scabs, and occurs chiefly on the hairy parts of the body. The scabs are less yellow and the eruption is less confluent than in *impetigo contagiosa*. A further degree of the ulcerative process constitutes *syphilitic ecthyma* and *rupia*.

Rupia.—This is a characteristic eruption, formed by large circular ulcers covered with greenish-brown scabs, which become piled up in a conical limpet-shell form as the ulcer increases in extent. Rupia is a late secondary or intermediate phenomenon of syphilis, and is seldom seen except in broken-down subjects, or in those who have neglected treatment.

Rupial ulcers, after healing, leave permanent round whitish cicatrices with a pigmented areola.

Papulo-ulcerative Syphilide.—This form of syphilide is distinguished from the ulcerative forms just described by the absence of secondary microbic infection. The process is one of rapid softening and ulceration of brownish papules, caused by intense action of the syphilitic virus. It is, in fact, a form of *malignant syphilis*. This syphilide may occur simultaneously on the skin and mucous membranes. The ulcers secrete a scanty sanious discharge, which dries in blackish-brown crusts.

Alopecia.—Syphilitic alopecia may be secondary to acneiform syphilides of the scalp, but more often occurs without visible lesions. According to Sabouraud, syphilitic alopecia is one of the infectious alopecias, and due to a toxin causing atrophy of the hair papillæ and death of the hair. The loss of hair may be diffuse or in patches, which sometimes coalesce, forming a polycyclic area which is characteristic of syphilis.

Diagnosis.—Syphilitic *alopecia* sometimes simulates *alopecia areata*, but in the latter the patches are larger, more circular, less numerous, and smooth like a billiard ball. In syphilitic alopecia the patches are smaller, more numerous, and more irregular—'like glades in a wood' (Fournier)—and there are generally a few scattered hairs left.

Syphilitic alopecia may affect the beard, moustache, and eyebrows. The latter are sometimes divided into sections, presenting an appearance as if snipped with scissors, which is characteristic of syphilis.

Regrowth of the hair is the rule in syphilitic alopecia, unless the papillæ have been destroyed by syphilides of the scalp extending to the hair follicles. These cases of atrophic post-papular alopecia generally affect the nape of the neck and the sides of the scalp.

The Nails.—The simplest form of syphilitic affection of the nail is constituted by a papule in the matrix. This causes an arrest of keratinization, resulting in loss of substance, denuding the bed of the nail, and causing partial or total detachment.

In *syphilitic onyxis* the nails may become cracked and friable, or much thickened, broken, and wrinkled. This condition

differs from psoriasis or eczema in preserving the form of the nail.

Perionyxis is more common. In the dry form there is more or less swelling of the bed of the nail, resembling a whitlow, but differing in its slower evolution, less pain, and in the absence of suppuration.

In some cases syphilitic perionyxis may ulcerate, penetrating to the roots of the nail, and causing destruction of the matrix.

Gummatous Syphilides.

Gummatous syphilides are characteristic of tertiary syphilis. They differ from secondary syphilides in causing destruction of tissue and the formation of scars, and in being less symmetrical, more circumscribed, and monomorphous. Pathologically, however, there is no sharp line of demarcation between secondary and tertiary syphilides, for they are both constituted by different degrees of the same morbid process. Moreover, there is no absolute clinical distinction, for, on the one hand, tertiary syphilides may occur in the first year of the disease in the form of what is known as malignant syphilis; on the other hand, secondary syphilides may appear several years after infection (delayed secondary syphilides), especially in the form of palmar and plantar syphilides.

The chief point of practical importance is the question of *contagion*. So far, the assumed pathogenic microbe of syphilis, the *Spirochæta pallida*, has been commonly found in secondary, but rarely in tertiary syphilides; but it is impossible to establish a sharp line between the contagious and the non-contagious syphilides.*

In tertiary syphilides the perivascular cell infiltration forms an inflammatory neoplasm in the skin, which has a tendency to soften or ulcerate. This process varies considerably in rapidity, some syphilides becoming ulcerative almost from the commencement, others ulcerating at one part and healing at

* Feulard has reported cases ot contagion from lesions having the appearance of secondary syphilides of four to twelve years' date.

others, pursuing a *serpiginous* course, which is characteristic of tertiary syphilides.

*Morbid Anatomy.**—The elementary lesion, or *syphilitic granuloma*, is constituted by an inflammation of nearly the whole of the dermis with perivascular nodules found round the vessels, which are affected with endo-periarteritis. The lesions are more diffuse than in the papule, the vessels more thickened, and there is more fibrous-tissue formation. The cells are similar to those of the plasmoma of the papule, and include large and small cells, epithelioid cells, and giant cells. The elastic tissue is more or less replaced by fibrous tissue. The epidermis becomes gradually atrophied. The evolution of the syphilitic granuloma is followed by a contractile cicatrix, by the gradual disappearance of the cellular elements, and their replacement by fibrous tissue. If the inflammation affects the superficial parts of the dermis, exudation of leucocytes is provoked by external irritation, and this exudation dries on the surface in the form of crusts (*crustate syphilides*).

Simple Gummatous Syphilide.—This is formed by dark red, copper or ham-coloured nodules of slow evolution. The elements may be discrete, and are often arranged in the form of a bouquet (Fournier); or they may be confluent, forming a placard which cicatrizes in the centre while extending at the periphery. The extending margin of this form of syphilide is *circinate* or *serpiginous*, and gives rise to the so-called 'geographical' figures which are characteristic of syphilis. After healing, a brown macule is left, which is followed by a depressed cicatrix. In this case there is destruction of subepidermic tissue without ulceration.

Ulcerative Gummatous Syphilide. — This varies very much in extent. It may consist of a small number of nodules forming one focus, or of a single nodule; on the other hand, it may form large placards, with extensive serpiginous ulceration. The evolution is slow and painless, and is not accompanied by inflammatory reaction or affection of the lymphatic

* Balzer uses the term 'syphilitic tubercle' for the elementary lesion of tertiary syphilides, but the term 'syphilitic granuloma,' which is used by Darier, is preferable, as avoiding confusion with tuberculosis.

glands. Owing to its insidious nature, it may be neglected by the patient and cause irreparable mutilation, especially when situated on the nose. It may undergo slow spontaneous resolution without treatment, but more often persists for many years. Under treatment it usually heals with remarkable rapidity. Recurrence is common, generally in other situations, more rarely in the scar.

The cicatrix after healing remains pigmented for a long time, but ultimately becomes white and more or less depressed. The shape of the scar is in accordance with that of the ulceration, and these circular, annular or arciform scars are valuable in the retrospective diagnosis of syphilis. When situated on the face these scars may cause deformities, such as ectropion, symblepharon, and destruction of the nose.

Phagedena may complicate ulcerative gummatous syphilides, constituting a form of malignant syphilis.

Syphilitic Elephantiasis.—Sometimes gummatous syphilides are complicated by a hyperplastic infiltration of the skin and subcutaneous tissue, constituting what has been called syphilitic elephantiasis. This is especially common on the labia in women, and sometimes leads to considerable hypertrophy. It may also affect the nose, resembling rhinophyma; the lower lip, constituting the hypertrophic syphiloma of Fournier; and sometimes the ears and limbs. Mauriac has described a similar condition affecting the face, which he named *syphilitic leontiasis*.

Sometimes the ulcerative syphilide develops exuberant granulations. This form, which is of no particular importance and very uncommon, has been designated *syphilitic frambœsia*, from its resemblance to yaws or frambœsia.

Diagnosis.—The chief differential diagnosis has to be made from *lupus* and *tuberculous ulceration*.

Lupus.—The dry gummatous syphilide differs from lupus: (1) In its dark red or ham colour; (2) in its greater hardness; (3) in the arrangement of its elements in the form of circles, rings, bouquets, crescents, or conjugate arcs. *Lupus* is of softer consistency, more irregular in configuration, and of a reddish-yellow colour. The characteristic 'apple-jelly' or

'barley-sugar' tubercle nodules can often be found at the periphery of the lesion, and are diagnostic.

Ulcerative syphilides sometimes simulate ulcerative lupus very closely. The chief points of difference are given in the following table:

	Ulcerative Syphilide.	Lupus.
1.	Areola brownish-red.	Areola rose-red or sometimes bluish.
2.	Borders well defined, sharply cut, hard, adherent, and infiltrated.	Borders thin, irregular, detached and undermined, and not infiltrated.
3.	Base depressed and covered with creamy yellow slough.	Base irregular, often on a level with the skin, and sometimes covered with exuberant granulations.
4.	Crusts hard, adherent, greenish-brown or bronze colour, and often stratified (rupia).	Crusts soft, fragile, less adherent, and of lighter colour
5.	Shape often circular, circinate, or serpiginous.	Shape irregular.
6.	Evolution more rapid.	Slower evolution.

None of these characters are absolutely constant, and cases sometimes occur in which a diagnosis can only be made by the therapeutic test. As a general rule, however, it may be said that syphilis makes as much progress in a month as lupus in a year. Other signs of syphilis or tubercle must be looked for to assist the diagnosis. It must, however, be remembered that both diseases may coexist in the subject, and that syphilis acts as a predisposing cause to tuberculosis. Both histological and bacteriological examination are uncertain, and inoculation of the guinea-pig is sometimes negative with lupus.

Ecthyma.—Simple ecthyma may resemble ulcerative syphilides, but is usually found in cachectic subjects, in those recovering from typhoid fever, etc., as a complication of scabies, pediculosis or varix, or as an occupational dermatosis.

Acne Necrotica.—This form of acne may be mistaken for syphilis, but differs in the following points: (1) Its predilection for the forehead, scalp, naso-genial furrow, sternal and interscapular regions; (2) its symmetrical distribution; (3) its

chronic nature and frequent paroxysmal outbreaks; (4) the redder and more inflammatory appearance of its elements; (5) its polymorphism; (6) its small and deep varioliform cicatrices; (7) the history of antecedent seborrhœa.

Sycosis.—Certain nodular forms of sycosis may resemble gummatous syphilides, but differ in being more inflammatory. Sycosis is a pustular folliculitis, and consists in an agglomeration of pustules centred by hairs; the syphilide, on the other hand, is formed by a coalescence of nodules. In trichophytic sycosis the fungus can be found.

Iodide Eruptions.—Some forms of iodide eruptions, commencing as vesicles or bullæ, may become covered with brownish crusts and closely resemble ulcerative syphilides. The chief points of distinction are the more rapid evolution; the commencement in vesicles, which can sometimes be found; the inflammatory areola and softer base; and the disappearance of the eruption after the drug is discontinued.

Bromide Eruption.—The administration of bromide sometimes gives rise to an eruption of condylomatous, circular, dark red papules, raised like a pastille on the skin. These may be isolated or united into placards, and when covered with brownish crusts may simulate syphilides. On removing the crusts, however, the base is simply eroded or vegetating, and has not the appearance of the syphilitic ulcer.

Cutaneous Gummata.—These are only further developments of the gummatous syphilide, as previously pointed out, and the term is usually applied to the circumscribed form of tertiary syphilide.

Gummata form cutaneous nodules, varying in size from that of a pea to that of a pigeon's egg. They are hard at first, but soon soften and break down into gummatous ulcers, which have the following characteristics: (1) The outline is circular, circinate, or polycyclic; (2) the ulcer is deeply excavated and crateriform; (3) the borders are cut sharply and vertically; (4) the edges are adherent and not undermined; (5) the periphery of the ulcer is infiltrated; (6) the base is covered with a caseous, adherent yellow mass, forming the gummatous core.

Cutaneous gummata may be single or multiple, and more than a hundred have been counted in the same individual. They are sometimes arranged in groups, and may be more or less symmetrical. They may occur on any part of the body, but are more common on the lower limbs.

When left to their own evolution they may cause extensive destruction of the soft parts, and even extend to the periosteum of the subjacent bones, and cause necrosis. Spontaneous resolution is rare, and the usual course is slow extension with partial cicatricial repair, resulting in contractile scars. Gummata often break down *in situ* after cicatricial repair. Gummatous ulceration may be aggravated by secondary infection, and in some cases becomes phagedenic.

Diagnosis.—Sometimes the cutaneous gumma, instead of discharging by a single opening, perforates the skin at several points. It may then be mistaken for a *carbuncle*, but the latter is more acute, more painful, and more suppurative. This form occurs chiefly on the buttocks.

Varicose Ulcer.—Gummatous ulceration of the legs is frequently mistaken for varicose ulcer when varix is present. The presence of varicose veins does not imply that an ulcer is varicose; moreover, varix is a predisposing cause of syphilitic ulcer by lowering the resisting power of the tissues. The varicose condition may also modify the evolution of the syphilitic ulcer, giving rise to a hybrid form, or *syphilo-varicose ulcer*. The chief differences between the varicose and syphilitic ulcer are as follows:

Varicose Ulcer.	Gummatous Ulcer.
1. Usually occurs on the lower part of the leg, especially about the malleoli.	Usually affects the upper part of the leg, around the patella.
2. Generally single.	Often multiple.
3. Irregular in form.	Circular or circinate.
4. Borders thick and rounded.	Borders sharply cut.
5. Base red or gray, sometimes diphtheroid.	Base covered with yellow caseous core.
6. Periphery pachydermatous, much pigmented, and often eczematous.	Often scars or other ulcers in neighbourhood.

Tuberculides.—Certain forms of tuberculides may resemble tertiary syphilides. The *erythema induratum* of Bazin, the tuberculous nature of which is doubted by Leloir and Vidal, is regarded by Bodin as either a 'scrofulo-tuberculous gumma,' or a gummatous syphilide of late heredo-syphilis. It is probably a hybrid lesion formed by tubercle and heredo-syphilis (scrofulo-syphilis).

Epithelioma.—Tertiary syphilitic ulceration has often been mistaken for malignant disease, and treated as such by excision. Fournier mentions several cases in which this mistaken diagnosis was made, but operation avoided by the timely intervention of antisyphilitic treatment. It is necessary to remember that tertiary syphilis may be limited to a single cutaneous lesion.

In the *epitheliomatous ulcer* the edges are harder and redder and the base more sanious. The ulcer is situated, not on an inflammatory infiltration, but on a tumour which extends both superficially and deeply. In epithelioma the corresponding lymphatic glands are soon implicated, whereas the syphilitic ulcer does not affect the glands. The diagnosis can usually be settled by microscopic examination; but if there is the slightest doubt as to the nature of the case, a thorough trial should be given to antisyphilitic treatment before having recourse to surgical measures.

Subcutaneous Gummata.

These develop as nodules of various sizes in the hypodermic tissue. They are hard, painless, and aphlegmasic, and are at first movable under the skin. Later on they undergo caseation and become adherent to the skin, which they perforate, constituting a *gummatous ulcer*, having the characteristics mentioned above. Subcutaneous gummata may occur on any part of the body, but are more common on the legs. They may be single or multiple, and occasionally occur in the form of diffuse placards of subcutaneous infiltration. After healing of the ulcer, a permanent depressed, pigmented scar remains.

Diagnosis. — Gummata differ from boils, carbuncles, or diabetic ulcerations in their slow and painless evolution without inflammatory symptoms. In their early stages they might be mistaken for lipomata or sebaceous cysts, but both of these are more circumscribed, more chronic, and do not go through the subsequent stages of the gumma with softening and ulceration.

The early stages of *cancer* differ in the more irregular form of the tumour, the early adherence to the skin, and the presence of pain. Later on the cancer forms a vegetating fungous tumour with everted edges, bleeding easily, and exuding a fœtid sanious discharge. In cancer the lymphatic glands are affected early; in gumma never.

The diagnosis from *varicose ulcer* is the same as that for cutaneous gumma mentioned above.

Treatment of Cutaneous Syphilides.

In addition to the general treatment for syphilis, certain local measures are useful in cutaneous syphilis. In extensive or chronic papular or gummatous syphilides, inunction with mercurial ointments often hastens their disappearance. If the patient is undergoing mercurial inunction, the parts chiefly affected by these syphilides should be chosen for the rubbing. Local inunction with mercurial ointment is especially useful in chronic plantar and palmar syphilides. In ulcerated syphilides, dressings with mercurial ointments (red or yellow oxide, calomel 1 in 10, or white precipitate) are useful. A 1 per cent. ointment of iodine also gives good results.

In gummatous ulcers, local calomel fumigation is a useful proceeding. This is carried out by means of a glass tube with a bulbous expansion in the centre. One end of the tube is drawn out to a fine point, and the other end attached to an indiarubber blower. The calomel is placed in the bulbous part of the tube and heated by a spirit-lamp; the calomel sublimes and the vapour is blown on to the sore, which it covers with a fine powder. Liquor sodæ chlorinatæ and iodoform are useful for extensive or phagedenic ulcers. Besnier recom-

mends injection of iodide of potassium into the substance of subcutaneous and cutaneous gummata, when these are of large size.

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CHAPTER VI

THE CIRCULATORY SYSTEM

SYPHILIS of the circulatory system, embraces nearly the whole of syphilis, since the great majority of syphilitic lesions are of vascular origin.

The Blood.

Syphilis acts on the blood in three ways: (1) By diminishing the number of red corpuscles; (2) by diminishing the proportion of hæmoglobin; (3) by increasing the number of white corpuscles. There also occur changes in size and form in the red corpuscles (poikilocytosis). Their resistance to cold is also diminished, which may explain the relation of paroxysmal hæmoglobinuria to syphilis. There is a relative increase in the number of mononuclear leucocytes and diminution of the polynuclear; also a slight increase in the number of eosinophiles, which is proportional to the intensity of the rashes. The serum is diminished in alkalinity and in chlorides.

The *Spirochæta pallida* is sometimes found in the blood, and has also been found in fluid obtained by blisters (Levaditi).

Syphilitic Anæmia.—The changes in the blood in syphilis are very variable, and constitute several different types. (1) The most usual form is *simple anæmia*, characterized by diminution in the number of red corpuscles, and proportional diminution in hæmoglobin. (2) In *chloro-anæmia* the diminution in hæmoglobin is greater than that accounted for by the smaller number of red corpuscles which may even remain normal in number. This type is common in females, and syphilis by itself may constitute *chlorosis*. (3) Chloro-anæmia

may be combined with leucocytosis. (4) In *Pernicious anæmia* the diminution in red corpuscles is much greater than that of the hæmoglobin; hence there is an apparent increase in the hæmoglobin. (5) The changes may be confined to the white corpuscles, constituting *leukæmia* or *leucocythemia*. It is more than possible that syphilis, especially hereditary syphilis, is the chief factor in the various leukæmias and polycythemias, which have been described.

Paroxysmal Hæmoglobinuria.—According to Balzer and others, both paroxysmal hæmoglobinuria and Raynaud's disease are due to general infective diseases, the chief of which is syphilis. Balzer reports an interesting case in support of this view. In a syphilitic subject affected with cyanosis of the nose and fingers these symptoms disappeared under treatment by injections of gray oil. Later on recurrence took place, together with paroxysmal hæmoglobinuria and the formation of a tubercular syphilide.

Whether the changes in the blood in syphilis are produced in the course of the second incubation or at the time of the eruptive outbreaks, the evolution is parallel to that of the eruptions, and subsides with the clinical symptoms of the disease, to recur at subsequent outbreaks. The intensity of the blood changes is proportional to the severity of the disease. In severe syphilis we find much diminution in the red corpuscles and hæmoglobin, and changes in form of the corpuscles; but it is impossible to distinguish between what is due to syphilis and what may be the result of associated symptoms, such as fever, etc., or of superadded infections. The first changes are however due to the specific infection.

The blood generally returns to its normal condition afterwards, but blood changes may persist as the only stigma of a latent infectious state. Changes in the blood are liable to recur, like all other syphilitic manifestations, and may be reproduced in the tertiary stage and in late hereditary syphilis.

Influence of Mercury on the Blood.—In syphilitic anæmia the administration of mercury restores the number of red corpuscles and the amount of hæmoglobin, and causes

leucocytosis to disappear. This reaction to mercury is the special character of syphilitic anæmia.

On the other hand, mercury, having restored the blood to its normal condition, becomes in turn an alterant. For a time it increases the hæmoglobin and the red corpuscles; later on it diminishes them. This indicates that mercury should only be given for short periods at a time, and lends support to the 'chronic intermittent treatment' of Fournier.

The Justus Blood Test.—The reaction of the blood to mercury was thought by Justus to be a test for doubtful cases of syphilis. This test is based on the idea that a single inunction of mercury in all untreated cases of syphilis causes a reduction of hæmoglobin, while in non-syphilitics no reaction follows. Justus states that the reduction is from 10 to 20 per cent., and occurs also after intravenous and subcutaneous injections, but not after ingestion of mercury by the mouth. David Jones has made a critical study of this test in 53 cases — 35 syphilitic and 18 control. The hæmoglobin was estimated by the specific gravity test. The syphilitic cases were divided into (*a*) 17 cases of active syphilis, not under treatment; (*b*) 1 case under treatment; (*c*) 2 latent cases; (*d*) 8 cases of chancre with adenitis. Of the 17 cases not under treatment, 13 responded to the test and 4 were negative. Of the 4 negative cases, 3 had characteristic syphilides. The latent cases and the case under treatment did not react to the test. Of the 8 cases with chancre and adenitis, 2 reacted and 6 were negative. The control cases included cases of phthisis, enteric fever, acute alcoholism, etc., and were all negative to the test.

The Justus test hence appears to be of doubtful value. The reaction may occur possibly in non-syphilitic affections, and often fails in latent cases and in chancre—in fact, in the very cases where diagnosis is specially required.

The Heart.

Syphilitic affections of the heart may be functional or organic, the latter including pericarditis, endocarditis, myocarditis, and gummata.

Nervous and Functional Changes.—The functional disorders of the heart which may be due to syphilis are of three kinds: (1) The expression of a neurosis developed under the influence of syphilis, such as hysteria, epilepsy, and neurasthenia; (2) irritation of the vagus of nuclear origin, or due to compression of the nerve by glands; (3) symptoms of commencing cerebro-spinal syphilis, such as tabes and general paralysis.

Cardiac Neurasthenia.—The first group is the most important, and is characterized by symptoms of palpitation, weak action of the heart, extracardiac murmurs, false angina pectoris, and intermittence. Clinically and pathologically this group may be divided into two types, the *asthenic* and the *hypersthenic*.

Asthenia is manifested chiefly by a weak cardiac impulse and pulse and palpitation. There may also be lipothymia, tachycardia, syncope, and intermittent action, and in severe cases a condition of 'fluttering heart.'

Hypersthenia, on the other hand, is characterized by cardiac erethism with a strong pulse, false angina pectoris, palpitation, and spasmodic mitral stenosis. The systolic impulse is increased, and there is pulsation of the vessels in the neck. The pulse has more the appearance than the reality of high tension. The second sound is accentuated. Functional murmurs may occur like those of chlorosis (which may itself be of syphilitic origin).

Palpitation differs from that of the asthenic type in being due to strong action of the heart, as opposed to weak action.

In severe cases there may be *pseudo-angina pectoris*. The latter is due to cardiac spasm, neuralgic in nature, and often a manifestation of a neuropathic or hysterical state connected with syphilis (Huchard). The pseudo-angina pectoris of neurasthenics has all the symptoms of organic angina, including precardiac pain, and pain down the left arm. But the pulse, instead of being small and intermittent, is strong and regular. Sometimes the skin over the cardiac region is hyperæsthetic.

Fournier mentions irregular and intermittent palpitations

occurring in secondary syphilis. 'Circulatory asthenia manifests itself by softness, smallness, and sometimes arythmia, of the pulse, dyspnœa, vertigo, and a tendency to lipothymia.' These neuro-cardiac phenomena are, however, only observed in the minority of cases of secondary syphilis.

Interstitial Myocarditis, or Cardiac Sclerosis.—This may be partial or diffuse. That syphilis can give rise to fibrous myocarditis without gummata was shown by Virchow in 1859, who described a case in which the right side of the heart was affected with gummata, and the left side with fibrous myocarditis only.

The morbid process is one of perivascular and intermuscular inflammation, originating in the small vessels and causing secondary degeneration of the muscle fibres. Mracek has shown that the vascular lesions sometimes begin in the intima and sometimes in the adventitia, and end ultimately in obliteration of the vessels. The cell infiltration is rapidly converted into organized connective tissue, which soon becomes fibrous and sclerous. Myocarditis and disorganization of muscular tissue may be established before functional disorders or anatomical lesions become apparent.

In addition to the vascular lesions of cardiac syphilis, changes in the nerve ganglia have been found by Braslawski. These changes are said to consist in round-celled infiltration of the ganglia and atrophy of the protoplasm of the nerve cells connected with interstitial sclerosis and obliteration of the small vessels supplying the ganglia.

Gummata.—Cardiac gummata may be miliary and only visible by the microscope, or they may form tumours varying in size from that of a pea to that of a pigeon's egg. They often project under the pericardium or endocardium, and are always separated from the cardiac muscle by a zone of fibrous tissue.

The first published case of gumma of the heart is due to Ricord. In this case, a man of forty-one, who died suddenly in the course of tertiary syphilis, multiple gummata were found in the walls of both ventricles, together with fibrous myocarditis and secondary pericarditis. There were also

gummata in the lungs. Since this case many others have been recorded.

Gummata of the heart are nearly always associated with fibrous myocarditis, and with thickening of the endocardium, causing valvular insufficiency or constriction; also with sclerosis of the coronary artery, which explains the frequency of sudden death, with or without angina pectoris. Gummata are more common in the left ventricle than in other parts of the heart.

Pericarditis. — In cardiac syphilis pericarditis is nearly always secondary to gummata of the myocardium, or to lesions of the subepicardial vessels. It may also be caused by syphilitic nephritis, in which case there may be pericardial effusion, or adhesions with their consequences.

Endocarditis.—How often the endocardium is affected by syphilis, and what part syphilis takes in the causation of valvular diseases of the heart, are questions which are impossible to decide, since a number of cases may be cured by antisyphilitic treatment without being recognised.

On this subject Huchard writes as follows: 'Syphilis only produces chronic lesions of this membrane. They comprise the two classic varieties, gummatous endocarditis and fibrous endocarditis. There are only a few observations published on gummata of the endocardium. Most often these are gummata of the myocardium with fibrosis of the neighbouring endocardium. As to syphilitic fibrous endocarditis, which is most often parietal, it may also occur on the valves. It then forms small grayish or yellowish nodules on the free borders of the valves—on each side of the nodules of Arantius, for example—or sometimes complete valvular sclerosis. The parietal form generally occurs at the base of the left ventricle at the septum, in the form of papillary excrescences or grayish, bluish, yellowish-white, firm and smooth thickenings. It is an open question whether these different lesions are syphilitic or only para-syphilitic, and also what connection they have with the lesions of arteriosclerosis.'

Dyce Duckworth has reported a case, in a man aged thirty-five, in which there was fibro-gummatous endocarditis and

myocarditis. Near the apex of the heart was a circular depression with thinning of the heart muscle, and the endocarditis was situated in this position. The patient died suddenly. There were also gummata in the lungs and other signs of syphilis.

Symptomatology, Diagnosis, and Treatment.—Syphilitic disease of the heart is more common than is generally supposed; in fact, syphilis must be regarded as the chief factor in heart disease, apart from rheumatism. It may be insidious in onset, and remain latent a considerable time without giving rise to symptoms, and then cause sudden death in persons apparently in the prime of life.

Extreme feebleness of the heart without dilatation, gradually increasing, in young or middle-aged persons who have had syphilis is suggestive of cardiac syphilis. Dilatation of either side of the heart may result from syphilitic fibrosis, and hypertrophy without any other obvious cause is probably due to syphilis. Apparently trivial signs of heart disease occurring in subjects who are known to have had syphilis should not be overlooked, and when occurring in the absence of a history of syphilis may be due to that cause, since a negative history of syphilis is no value whatsoever in the formation of a rational diagnosis.

The *Symptomatology* is very varied, and is formed by signs connected with lesions of the vessels, cardiac muscle, endocardium and pericardium, and by symptoms due to the pressure of gummata. In some cases latent cardiac syphilis, when associated with changes in the cerebral vessels, may end suddenly with cerebral symptoms. When renal lesions coexist with cardiac syphilis there is dyspnœa of renal origin.

Huchard remarks that, 'apart from all superadded signs depending on concomitant cerebral, hepatic, or renal lesions, the symptomatology of gummatous cardiac syphilis realizes the clinical picture of myocardiac insufficiency or hyposystole, to which patients succumb more or less slowly, generally in the absence of lesions of the orifices. At other times arterial lesions coexist, either of the aorta or coronary arteries, creating a clinical type shown by the following observation: A patient

with ulceration of the palate presented signs of tricuspid and aortic insufficiency, and died from asystole with pulmonary œdema. At the autopsy gummatous myocarditis, chronic aortitis with lesions of the sigmoid valves, and slight pericardial and abdominal effusion were found (Graeffner). At other times to the signs of myocardiac insufficiency are added painful symptoms resembling angina pectoris; the patient dies rapidly, and at the autopsy, besides subpericardial and subendocardial gummatous nodules, and large gumma of the interventricular septum, there is found arteritis of the coronary arteries (Henderson).

Sudden death is common in cardiac syphilis, and Huchard has collected thirty-five cases due to different causes: often to sclerosis of the coronary arteries or to aortic lesions; sometimes to rupture of the heart by an infarct; more rarely to rupture of the aorta, aneurism, embolus of the carotid, rupture of a gumma into the heart, paralysis of the heart by myocarditis, or to complex lesions caused by arterial obliteration and pressure of gummatous masses in the sigmoid region of the aorta and base of the pulmonary artery; sometimes to pressure of gummata in the walls of the heart, and especially in the septum.

A good example of sudden death from cardiac syphilis is given by Sydney Phillips:

'A professional man, aged fifty-three, who in his youth contracted syphilis, had from time to time been troubled with sores on the tongue, and in 1890 suffered from epileptiform convulsions, which gradually ceased to occur. In 1894 he was suddenly taken ill in the night. He was walking about the room in an agony of pain, which he described as unendurable. The lower parts of the sternum and epigastrium were the chief seats of pain, which went through the back and also extended down the left arm; there was no marked pallor, no cyanosis, and no laboured breathing; the pulse was sixty, and laboured; there were no signs of valvular mischief. Recovering under the free administration of morphia, he returned to town and to work against medical advice; but eighteen days after this attack of pain, on returning home from business, he quietly expired in an armchair while reading the evening paper.'

At the post-mortem a gumma the diameter of a two-shilling piece was found in the left ventricle.

This is a good illustration of syphilis of the heart, and no doubt explains many cases of sudden death from 'heart failure,' which are only too common. The existence of latent cardiac syphilis may also account for some of the cases of death under anæsthetics.

Diagnosis.—This is in some cases impossible, owing to the diversity in the symptoms. Huchard concludes that, while 'cardio-sclerosis and myocarditis manifest themselves only by symptoms of cardiac insufficiency, syphilitic cardio-sclerosis and myocarditis manifest themselves not only by these symptoms, but also by all those due to concomitant aortitis, sclerosis of the coronary arteries, pericarditis, and also to renal or hepatic manifestations. Therefore *associated symptoms*, joined to antecedents of syphilis, should form the basis of the diagnosis.' He also remarks that dilatation of the heart, without evidence of valvular disease, is suggestive of syphilis.

Treatment.—According to Huchard, apparently irremediable cases of cardiac syphilis may be cured by early and energetic treatment. The treatment he suggests is by weekly injections of gray oil, combined with the internal administration of iodide of potassium in daily doses, increasing from 30 to 90 grains. A lacto-vegetarian diet is also indicated, as there are usually coexisting kidney lesions. Digitalis is also useful as an additional medicament.

The two following successful cases are mentioned by Huchard as examples:

1. A patient, aged thirty-seven, with syphilis of eleven years' date, presented subcutaneous gummata, followed by the following cardiac symptoms: dyspnœa, palpitation with slight arythmia, signs of dilatation of the heart without any murmur, anginal pain; then signs of myocardiac insufficiency with weak pulse, and œdema of the lower limbs. Cardiac syphilis was diagnosed and energetic antisyphilitic treatment instituted. In less than six months all these severe symptoms had disappeared, and the patient was considered as cured of the heart affection.

2. A woman, aged forty-one, in whom syphilis was suspected without being confirmed, presented associated cardiac and cerebral symptoms, including vertigo, slow pulse, epileptic attacks, hyposystolic state of heart, with dilatation without valvular lesions. All these symptoms disappeared under treatment.

Angina Pectoris.

'The anatomical cause of angina pectoris is a lesion of the aorta situated near the orifices of the coronary arteries, or a lesion of the coronary arteries, with or without aortitis, leading to diminution in their calibre or obliteration of their lumen. By this definition angina pectoris is clearly separated from all cardiac or extracardiac pains, which are often confounded with it. The proof of its arterial origin being now established, it is more in accordance with the truth to say that *there is only one angina pectoris*. All other painful manifestations of the cardiac region should be ranged in the category of *precordialgias*, neuralgic affections of the cardiac or periaortic nerves. Both from the nosological and clinical points of view they are absolutely different from angina pectoris; they are, rather, *pseudo-anginas*, to which it would be preferable to give the following designations: neuralgia of the heart or of the precordial region, cardialgia, cordiodynia, precordialgia' (Huchard).

From this definition it follows that true angina pectoris must in most cases be due to syphilis, since this is the most frequent cause of disease of the coronary arteries and aorta. Huchard places syphilis among the chief causes of angina pectoris, and points out that the etiology of this condition is the same as that of arteritis.

Syphilitic angina pectoris may be due to acute or chronic arteritis of the aorta or coronary arteries. The former may be rapidly cured by specific treatment; but a cure is much more difficult to obtain when there are chronic lesions of the vessels, or when there is thrombosis of the cardiac arteries.

Diagnosis.—The classical symptoms of angina pectoris are sudden agonizing pain behind the mid-sternum occurring after exertion, a sense of impending death, pain radiating down the left arm to the fourth and fifth fingers, and high arterial tension, the whole attack lasting only a few minutes. The patient holds his breath during the attack, but there is no true dyspnœa.

Sometimes the radiating pain affects both arms, and occa-

sionally only the right arm; it may cease at the shoulder or elbow, or may affect the fingers only. Vasomotor phenomena may also occur, causing blanching of the face and local asphyxia of the fingers. In cases where there is disease of the coronary arteries without aortitis or arterio-sclerosis the arterial tension may be normal, or even lowered. This accounts for the uncertain action of nitrite of amyl, which only relieves those cases in which arterial tension is raised. In abnormal cases the substernal pain may occur alone, without radiating to the arm; and in other cases the pain may be limited to the left arm, but absent in the chest.

The differences between true angina and pseudo-angina are given by Huchard as follows: '(1) All angina pectoris produced by any effort, such as rapid walking, is a *true or coronary angina*. (2) All angina pectoris produced spontaneously, without the intervention of an action necessitating an effort, is a *false or neuralgic angina*. (3) When a patient having attacks caused by effort has them spontaneously during the night, the first law holds good—it is always a true angina. (4) Thoracic pains provoked by pressure are not anginal pains.'

It is beyond the scope of this book to discuss the reasons for and against the distinction between true and false angina pectoris, and the various theories which have been propounded to explain these phenomena. It is sufficient for our purpose to adopt the views of Huchard, and to regard angina pectoris with organic lesions as due to syphilitic disease of the heart, aorta, or coronary vessels. It is necessary to point out that alleged cases of true angina pectoris, without organic disease of the vessels, require post-mortem verification before they can be accepted.

Treatment.—Syphilis being admitted as the chief cause of true angina pectoris, it is obvious that energetic antisyphilitic treatment should be tried in such cases. It would also appear to be worth a trial in doubtful cases where there is difficulty in arriving at a conclusion as to whether the case is one of true or false angina.

Dieulafoy has reported several cases of angina pectoris, due to syphilitic disease of the aorta, which were relieved by injec-

tions of biniodide of mercury. In one case the patient was free from symptoms seven years after this treatment. He points out that mercurial injections often cause the anginal symptoms to disappear, although the organic lesion may be beyond repair. Dieulafoy's practice in such cases is to inject daily from ½ up to 2 centigrammes of biniodide of mercury in aqueous solution, for series of ten to twelve injections, separated by a fortnight or a month's rest.*

Syphilitic Arteritis.

Changes in the bloodvessels constitute the fundamental element in the pathology of syphilis, and therefore require to be considered in detail.

Syphilitic arteritis was described by Dittrich in 1849, by Virchow in 1859, and by Lancereaux and Gros in 1861. The effects of syphilis on the cerebral arteries was pointed out by Wilks, Moxon, Hughlings Jackson, Bristowe, and Fournier. Heubner, in 1874, described endarteritis obliterans, which is now known to be only one of the forms of syphilitic arteritis.

Etiology.—The arterial walls being constantly bathed by blood, which is altered in constitution by the microbe of syphilis or its toxins, is often affected by modifications in structure, constituting arteritis. This fact is not peculiar to syphilis, for nearly all the acute and chronic infections (enteric, variola, diphtheria, scarlatina, pneumonia, malaria, tubercle, etc.) are said to cause reaction or degenerative changes in the walls of arteries. The same effects have been attributed to gout, alcohol, and lead-poisoning. It is therefore apparent that other causes than syphilis may take part in the causation of arteritis, and in many cases it is impossible to attribute to each its real value. However, syphilis may be regarded as

* It is interesting to note, by the way, that the great John Hunter suffered from angina pectoris, and died during an attack. Extensive disease of the aorta and coronary arteries was found at the autopsy. Hunter's famous inoculation of himself with syphilis in his attempt to prove the identity of syphilis and gonorrhœa is well known, and there can be little doubt that this unfortunate experiment was the cause of his death from syphilitic arterial disease.

the chief cause of arterial disease, and the other factors are probably in many cases only of secondary importance.

Arteritis occurs in primary syphilis, where it causes infiltration and thickening of all the coats of the vessels of the chancre. According to the recent researches of Rieder, these changes are preceded by alterations in the veins and lymphatics. This arteritis takes a large part in constituting the induration of the chancre.

'In all the secondary and tertiary manifestations, whatever their nature and situation, endo-periarteritis is the most constant and most characteristic element of the lesions. Recent research has shown that phlebitis also plays an important rôle, but without retracting from that which has long been attributed to lesions of the arteries and arterioles. To study syphilitic arteritis in its widest sense is to deal with the whole pathology of syphilis' (Darier).

The date of appearance of syphilitic arteritis of the larger arteries, or 'pure syphilitic arteritis,' is generally between the third and twelfth years of the disease; but lesions of the aorta are generally delayed till the fifteen or twentieth years. However, syphilitic arteritis of the cerebral vessels may appear in the first year, and Darier has recorded two cases of fatal cerebral arteritis at eight and nine months respectively after infection. In fact, the arterial lesions of syphilis show that there is no didactic distinction between the secondary and tertiary periods of the disease.

Pathological Anatomy. — The lesions of syphilitic arteritis visible to the naked eye are partial and segmentary. The cerebral arteries are most commonly affected, especially those forming the circle of Willis, the internal carotid, the anterior cerebral, the Sylvian, the vertebrals, basilar and posterior cerebral. The vessels are irregularly thickened and covered with white patches, often thrombosed, obliterated at some places and distended at others. Fusiform or saccular aneurisms may result, which may undergo obliteration or may rupture. Moxon has compared the appearance of syphilitic arteries to that of boiled macaroni. These changes in the cerebral arteries are accompanied by exudative meningitis of the neigh-

bouring meninges. After the cerebral vessels, *the aorta* is most often affected, generally near the aortic valves. Syphilitic aortitis often causes aortic regurgitation and aneurism of the coronary arteries.

Histology.—The following description is that given by Darier from examination of the cerebral arteries: In these vessels there are certain peculiarities in structure which require mention: the intima is thin and fibrillar, the adventitia has no longitudinal fibres, the internal elastic lamina is clearly defined, but the external elastic lamina is wanting.

The *intima* is always thickened, generally concentrically, but sometimes more on one side than the other. The first change in the intima consists in an infiltration of round cells, which later on become stellate, anastomosing in a network enclosing a gelatinous substance. In some cases circumscribed masses of cells, or microscopic gummata, containing giant cells, have been found in the intima. The internal elastic lamina generally remains intact, but it may be interrupted or absorbed.

The *adventitia* is always more or less affected and infiltrated with round cells. The vasa vasorum of the adventitia are themselves thickened, and according to Rumpf the origin of the whole inflammatory process lies in the vasa vasorum.

The *tunica media*, which is normally destitute of vessels, is only affected when the intima and adventitia are profoundly altered. When this takes place, the muscle cells are atrophied and replaced by embryonic connective-tissue cells, and the vessels of the adventitia penetrate the middle coat. When all three coats of the artery are disorganized in this way, the condition is known as *panarteritis.*

The arterial wall, being deprived of its elastic and muscular elements, offers less resistance to the pressure of the blood, and progressive bulging takes place, leading to the formation of fusiform or saccular aneurisms. There may be a 'dissecting aneurism,' when a cleavage in the wall allows infiltration of blood between the different layers, generally between the internal elastic lamina and the modified middle coat.

Varieties.—In the *endarteritis obliterans* changes in the intima

predominate, and, according to Heubner, the stellate cells which form in the intima are derived from proliferation of the endothelial cells. In the *periarteritis* of Baumgarten there is a diffuse nodular perivascular infiltration round the vasa vasorum of the adventitia, and in this form gummatous nodules containing giant cells occur (periarteritis gummosa). In *panarteritis*, in which all the coats of the vessel are altered, there is sometimes acute diffuse inflammation, sometimes fibrous transformation, which forms the histological substratum of aneurism.

It must, however, be borne in mind that the subdivision of syphilitic arteritis into these different types is somewhat artificial, for these different forms may all be met with in the same subject, and they have insensible transitional forms between themselves. The usual type met with is a combination of endarteritis and periarteritis, or *endo-periarteritis*.

Bacteriology.—The *Spirochæta pallida* has been found in the walls of vessels affected by syphilitic endo-periarteritis and in the perivascular infiltration. Colonies of spirochætes have also been observed in the terminal parts of the vessels (Levaditi).

Pathological Physiology.—Thickening of the intima causes ischæmia of the parts supplied by the vessel, or anæmia if there is complete obliteration by thrombosis. The result will depend on whether the artery is a terminal one, or whether there is collateral circulation. In the latter case the circulation is only impeded, causing diminished function. In the case of a limb this will be manifested by temporary weakness and intermittent claudication; in the case of the coronary arteries it may cause angina pectoris on exertion or emotion; in the brain it will cause dizziness or temporary paresis.

Occlusion of a terminal artery, or different branches supplying the same area, will cause arrest of function and necrobiosis. In the cerebral arteries this will lead to softening, varying in extent according to the vessel affected, and manifested by various forms of paralysis, dementia, aphasia, etc.

Gangrene.—Syphilitic arteritis affecting the vessels of the lower limbs may lead to gangrene, and cases of so-called

'senile gangrene' occurring in middle-aged subjects are usually due to syphilis. The premonitory signs consist in pain, which may persist for weeks or months without other signs than weakness and algidity; sometimes cyanosis, œdema, and anæsthesia. A certain sign of arterial constriction, according to Charcot, is 'intermittent claudication,' or limping, which occurs during an effort. While walking there is a sudden attack of numbness, weakness, and pain in the limb, with cramp and stiffness, which passes off after a rest. The calibre of the artery is enough to carry on the nutrition of the limb during repose, but does not allow enough blood-supply for muscular work. Further constriction of the vessel causes the same symptoms during repose, together with algidity, œdema, anæsthesia, and finally cyanosis and gangrene. Gangrene is usually progressive, beginning in one of the toes and extending to the foot. In some cases syphilitic arteritis may be the cause of tertiary phagedena.

Atheroma and Arterio-sclerosis.

Atheroma.—The characters which are usually mentioned as differentiating atheroma from syphilitic arteritis are the greater extent of the lesions, which in the cerebral arteries may extend to the finest ramifications; the predominance of the lesions at the points of bifurcation of the arteries; the elongation of the vessels, causing them to become tortuous; and the tendency to fatty and calcareous degeneration, which sometimes converts the vessels into rigid tubes.

It has, however, been shown by Hippolyte Martin (1881) that the first change in atheroma is *endarteritis obliterans of the vasa vasorum* (endo-vascularitis), which causes obstruction to the nutrition of the walls of the larger vessel, with consequent fatty degeneration, or 'atheroma.' Now, since syphilis is the chief cause of endarteritis obliterans, it is obvious that it must be a cause of atheroma. Mott points out that atheroma of the aorta in young subjects is presumptive evidence of syphilis, and the same will apply to atheroma of other arteries. In fact, atheroma is a secondary degeneration of

the coats of an artery caused by syphilitic endarteritis of its vasa vasorum.

Arterio-sclerosis.—Huchard regards atheroma and arterio-sclerosis as due to the same morbid process—'atheroma is a lesion, arterio-sclerosis the disease.' He concludes that 'in the evolution of generalized arterio-sclerosis two anatomical periods can be distinguished—(1) the development of endo-vascularitis, or primary endarteritis of the vasa vasorum; (2) nutritional disorders, which are the consequence of it, and which lead to arterial sclerosis on the one hand, and visceral sclerosis on the other hand. Arterial sclerosis (atheroma) is nothing else than a dystrophic sclerosis of the vascular tunics, consecutive to endarteritis obliterans of their nutrient vessels.'

Huchard, although admitting the relation between syphilis and atheroma, states that atheroma of syphilitic origin is rarely generalized, and hence he does not regard syphilis as one of the usual causes of general arterio-sclerosis. However, George Oliver comes to the conclusion that 'observations point to a general arteritis as the ordinary effect of the syphilitic infection, the intima of the whole arterial tract being involved.'

Mott also states that syphilitic arteritis sometimes 'gives rise to a general affection of the small arteries and arterioles.' Again: 'No disease is probably more productive of arterial degeneration than syphilis, and this in several ways—(1) by causing endarteritis of the vasa vasorum, and defective nutrition of the walls of the large arteries; (2) by the devitalizing influence of a toxin, long present in the body, producing anæmia and lowering the physiological margin of normal metabolism, so that in case of injury or strain of a tissue the equilibrium is not maintained, and degeneration ensues.'

It would appear rational to regard generalized arterio-sclerosis as a *parasyphilitic* phenomenon. In this way we may look upon syphilis as having a twofold action on the vascular system — (1) the production of syphilitic arteritis and atheroma of more or less irregular distribution; (2) a more general process of arterio-sclerosis affecting the whole of the arterial system, and due to parasyphilis.

It is impossible to judge of the relative value of the other alleged factors in the production of arterio-sclerosis, but a few remarks may be made concerning the more important of them.

Huchard puts gout, chronic rheumatism, gouty diabetes, saturnism, alimentary toxins, senility, and possibly the remote results of acute fevers, among the certain causes of arterio-sclerosis; and syphilis, alcohol and malaria among the doubtful causes. He also states that generalized arterio-sclerosis is often hereditary. It would, however, appear more probable that the condition which causes the arterio-sclerosis is hereditary, and that this may be syphilis. Most of us would regard senility as the result, rather than the cause, of arterio-sclerosis; and as to saturnism, the number of persons affected with lead-poisoning must be infinitesimal compared with the number of syphilitics.

Alcohol is known to aggravate syphilitic lesions, and it is highly probable that the majority of cases of arterio-sclerosis are due to the combined effects of syphilis and alcohol, and that other causes, such as gout and alimentary toxins, are subsidiary. In this connection the following words of Darier are worth quoting:

'Without departing from the reserve which is necessary in forming a decision on such a difficult subject, we may admit that atheroma and arterio-sclerosis are very probably related to diverse infections on the one hand and to intoxications on the other hand, either from exogenous poisons or from endogenous poisons, arising, for example, from functional disorders of the intestine, excretory organs, or glands of internal secretion. Whether we are concerned with a common arteriopathy due to multiple causes, or with different chronic arterites or arterial degenerations which we have not yet differentiated, is of little moment. I think that among the multiple causes of this arteriopathy it is not irrational, but, on the contrary, admissible and plausible, to include syphilis, acting directly or indirectly by organic lesions which it has caused.'*

* See also remarks on Suprarenal Gland in Chapter XVII.

Aortitis and Aneurism.

Syphilitic endarteritis of the vasa vasorum of the aorta is the principal cause of chronic aortitis, atheromatous degeneration of the aorta, and aneurism. Syphilitic aortitis is also a cause of aortic stenosis and aortic regurgitation by implication of the valves.

Deguy, on post-mortem examinations of undoubtedly syphilitic subjects, found all varieties of chronic aortic disease, including fibroid aortitis, soft atheroma, and calcareous deposits; sometimes the wall of the artery was thickened, at other times it was atrophied; the lesions were sometimes localized and sometimes diffuse. A form of *acute syphilitic aortitis* has been described by Letulle in which there was diffuse cell infiltration of all the coats of the artery, apparently originating in the vasa vasorum of the adventitia. The elastic tissue was destroyed, and replaced by newly-formed tissue of low vitality.

Aneurism.—Although the syphilitic origin of aneurism was described by Fernel in 1554, and later on by Ambroise Paré and Morgagni, it was not fully recognised till Welch in 1875 published the results of his examination of soldiers affected with aneurism. In these cases Welch found obvious evidence of syphilis in 50 per cent., and probable syphilis in some others. Since then Etienne, in an analysis of 376 cases of aneurism, found evidence of syphilis in 70 per cent. Included in Etienne's statistics were thirty-eight popliteal and eighteen femoral aneurisms, conforming with the classical description of so-called 'spontaneous aneurism' described in the text-books on surgery.

The arguments in favour of the syphilitic origin of aneurism are—(1) the large percentage of cases in which there is evidence of syphilis; (2) the frequent coexistence of aneurism with other syphilitic lesions, especially with other lesions of the vascular system, such as cerebral syphilitic arteritis; (3) the frequency of aneurism in the subjects of tabes dorsalis, which is now known to be of syphilitic origin; (4) the com-

paratively common occurrence of aneurism among prostitutes, whereas women as a rule are seldom affected by it.

The old argument against the syphilitic origin of aneurism —the usual failure of antisyphilitic treatment—is of no weight, because by the time the aneurism is developed the damage is already done and the lesion beyond repair by drugs. As Huchard says, 'Although iodide and mercury may cure aortitis, syphilitic arteritis, and arterial swellings in their *pre-aneurismal* period, these drugs often have no action on syphilitic aneurisms when fully developed, for the following reasons: Arteritis is at the same time syphilitic in origin and in nature, which explains the efficacy of treatment; aneurism may be of syphilitic origin, but has lost its anatomical specific characters, and enters into the category of the *parasyphilitic* manifestations described by Fournier (tabes, general paralysis, etc.) which usually resist medication. Therefore, early and intensive treatment is indicated as soon as the existence of ectasial or obliterative arteritis is discovered in a syphilitic.'

It is also probable that *heredo-syphilis* may give rise to aneurisms. Huchard mentions two cases in which he found aortic aneurism in the subjects of hereditary syphilis, aged eighteen and twenty-two respectively.

The Veins.

Endophlebitis.—Rieder showed that endophlebitis occurred in association with lymphangitis in the primary chancre, and considered that these conditions preceded changes in the arterioles.

In secondary syphilis phlebitis sometimes occurs, chiefly affecting the internal and external saphenous and the median basilic and cephalic veins. It usually assumes a benign form, without much inflammatory reaction or œdema, and may affect the vein in its continuity or in segments. In an autopsy made by Mendel and Thibierge endophlebitis was found.

Nodular Phlebitis.—Jullien and others have described a somewhat rare form of phlebitis associated with gummatous

nodules surrounding the veins. This is of interest in connection with *erythema nodosum*, which it resembles both clinically and pathologically. Erythema nodosum is regarded as a manifestation of different infections, and the pathological changes occurring in the lesions resemble those of thrombo-gummatous phlebitis. The regions affected are the same in both cases—viz., the legs, thighs, and arms—and the lesion takes the form of a hard bluish swelling in each case. Syphilis is therefore probably one cause of erythema nodosum, and according to Jullien this condition signifies severe syphilis. In a case of the author's, lesions, having the characteristic appearance of erythema nodosum appeared on the legs in a girl suffering from secondary syphilis, and disappeared under mercurial treatment. Sometimes the lesions break down and ulcerate, and according to Blaschko most syphilitic ulcers commence by periphlebitis.

Gummatous Phlebitis.—Circumscribed gummata in the walls of the veins have been described by several observers. Dowse reported the case of a large gumma involving the tentorium cerebelli, and causing obstruction to all the venous sinuses except the occipital.

Gummatous phlebitis of the portal vein has been found in newly-born syphilitic infants.

The Lymphatics.

Lymphangitis.—In the course of secondary syphilis the lymphatics may sometimes be felt as hard, painless cords, usually without any acute inflammatory symptoms. This condition sometimes occurs in the glandulo-preputial furrow, forming nodular and sometimes moniliform indurations. If the mucous membrane covering these nodules becomes eroded, they may resemble chancres. Fournier calls these *lymphangitic pseudo-chancres*, and says they may be mistaken for recurrent chancres, or even for cases of reinfection.

Plastic Lymphangitis.—This probably causes the condition of so-called 'syphilitic elephantiasis,' which is often found affecting the labia in women (see Chapter IX.).

Adenitis.—Enlargement of the lymphatic glands almost

always occurs in secondary syphilis, and constitutes one of the most valuable aids to diagnosis. It chiefly affects the posterior cervical and suboccipital glands, but may also occur in the anterior cervical, axillary, and inguinal glands. There is a popular idea that the epitrochlear gland, above the inner condyle of the humerus, is often affected; but according to Fournier the importance attached to this symptom has been much exaggerated.

According to Augagneur and Landowzy, enlargement of the lymphatic glands in secondary syphilis is a sign of reaction of the organism against the attack of the syphilitic virus, and a considerable degree of enlargement of the glands is therefore a favourable sign, as giving evidence of active defence. However, this idea does not appear to be supported by clinical evidence, because in many cases of malignant syphilis the glands are much enlarged, and in cases of benign syphilis their enlargement is often slight. In fact, there does not appear to be any definite relation between the gravity of the syphilis and the degree of glandular enlargement.

Scrofulo-Syphilis. — In tuberculous subjects syphilitic adenitis may be the exciting cause of strumous glands, by constituting a kind of hybrid lesion, partly tuberculous and partly syphilitic (Ricord's 'scrofulate de vérole'). This condition, according to Fournier, is more common than is generally supposed, and probably accounts for many of the strumous glands so common in children. In this case the hybrid would be between heredo-syphilis and tuberculosis. The subjects are not always of the 'strumous' type, and may be apparently of healthy constitution.

Scrofulo-syphilis probably accounts for some cases of *retro-pharyngeal abscess*, by affecting the posterior pharyngeal glands.

The Spleen.

This organ, which is commonly enlarged in heredo-syphilis, may be also affected in secondary acquired syphilis; but the amount of enlargement does not appear to have any relation to the severity of the disease.

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CHAPTER VII

THE ALIMENTARY SYSTEM

PRIMARY chancres of the lip, tongue, and tonsil have been described with the extragenital chancres. Syphilitic affections of the teeth are described with hereditary syphilis.

I. The Mouth and Pharynx.

Secondary syphilis affects the buccal cavity in the form of erythema and mucous patches, and tertiary syphilis in the form of gummatous infiltration and ulceration.

1. Secondary Syphilis.

Erythema.—Secondary erythema of the throat is an early and characteristic sign. It may consist only of a variable degree of diffuse erythema affecting the oro-pharynx ; or may form a deep red arch, including the tonsils, fauces, and soft palate, sharply defined from the hard palate, which appears rather paler than usual. The tonsils are often red and swollen, and the mucous membrane has an opalescent appearance in the early stage of inflammation.

Mucous Patches.—The mucous patch, or mucous syphilide, is the commonest and most contagious of all the syphilitic lesions (Fournier). It is the homologue of the papular or papulo-erosive syphilide of the skin, and differs from it only on account of its situation. The thickened epithelium, owing to the warmth and moisture of the parts, becomes sodden, giving rise to various appearances according to the degree of epithelial thickening and the amount of erosion.

Mucous patches are predisposed to and aggravated by neglect of the hygiene of the mouth, decayed teeth, alcohol, and excessive smoking. They may occur in any part of the buccal cavity, but have a predilection for the tonsils, tongue, and lips; they are less common on the palate, cheeks, and gums, and rare in the pharynx.

Fournier divides mucous syphilides into four classes: erosive, papulo-erosive, papulo-hypertrophic, and ulcerative. These differ only in the degree of the inflammatory process, and are often found together. In the earliest stage they appear as bluish-white, gray, or opaline spots, varying in size, and situated on the congested mucous membrane. They have been compared to drops of milk glued to the mucous membrane. They may be few or multiple, and are often symmetrical and confluent, sometimes forming a complete circle, including the pillars of the fauces, base of the tongue, and soft palate. A string of confluent mucous patches in their early stages has been compared to a 'snail-track.' According to the degree of erosion, the mucous patch varies in appearance, being sometimes red in the centre with a gray circumference, sometimes gray with a red areola.

Mucous patches are sometimes covered with an exudation resembling the false membrane of diphtheria. These diphtheroid mucous patches are most often seen on the tonsils, lips, and tongue; seldom on the soft palate, uvula, or pharynx, and thus differing from diphtheria. Occasionally they may be accompanied by fever and laryngitis, etc., and Fournier mentions an instance in which a surgeon was called in to perform tracheotomy on a supposed case of diphtheria which turned out to be secondary syphilis.

Buccal syphilides may be situated partly on the mucous membrane and partly on the skin, forming a red erosion on the former and a crusted syphilide on the latter. When situated on the buccal commissures, they form two opposed patches, separated by a painful furrow at the corner of the mouth.

On the *tongue* the mucous syphilides assume several forms: (1) Small red or gray erosions on the sides or tip of the

tongue. (2) Radiating fissures on the back of the tongue. (3) Smooth bald patches (*glossitis depapillans*), caused by the loss of the horny prolongations of the papillæ. These bald patches may extend over half the tongue; they are always dry, unless complicated by secondary irritation, and thus constitute dry mucous patches. (4) At the back of the tongue the mucous patches may assume the hypertrophic papular form or condyloma. The *ulcerated mucous patch* occurs in the form of round or ragged ulcers, chiefly situated on the tonsils and fauces.

The *Symptoms* of mucous patches vary much in different subjects, and also according to their situation; they may cause no symptoms and remain ignored for a long time, or, when situated on the tip of the tongue, may cause pain during mastication. They are irritated and congested by tobacco smoke, especially in the form of cigarettes, and by hot food or spices, etc. Mucous patches are extremely contagious and liable to recur, even after several years, and the patient should be warned of the danger of conveying infection by kissing, and by spoons, tobacco-pipes, and other things inserted into the mouth. It is important to examine the throat and mouth in every case of syphilis.

Diagnosis.—1. From *diphtheria*, the diphtheroid mucous patch may be diagnosed by the absence of the Klebs-Loeffler bacillus; by the constitutional symptoms being as a rule much slighter, and by the coexistence of other secondary syphilides of the skin and other signs of syphilis.

2. *Buccal herpes*, analogous to genital herpes, sometimes occurs on the sides of the tongue in the form of small gray spots, which become eroded and are preceded by neuralgic pains in the tongue. These spots differ from mucous patches in their polymicrocyclic outline and in the presence of a collarette of epithelial débris formed by the remains of the broken vesicle. Fournier states that they generally follow buccal syphilides, and regards them as metasyphilitic in nature. They do not react to mercurial treatment.

3. *Aphthæ* are distinguished by their orbicular outline, yellow colour, cup-shaped depression, and bright red border in their

early stage. They commence in the form of a small pustule, which soon becomes ulcerated, and are very painful on every movement of the tongue. The mucous patch, on the other hand, is a flat erosion of a red or gray colour.

4. *Buccal hydroa* is an affection of the lips and tongue, consisting of bullæ, which burst and leave an erosion covered with detached epithelium, the size of a lentil or almond. When situated on the tongue, the normal papillæ are absent. The broken bullæ closely resemble mucous patches, but differ in being redder and more inflammatory, in the pseudo-membranous collarette of epithelial débris, and sometimes the coexistence of a bullous eruption on the skin.

5. *Perlèche*, the impetiginous lesion affecting the commissures of the lips, may resemble mucous patches in the same situation. It occurs in epidemics in children, usually from sucking pen-holders, and is rare in adults except when contracted from children. The lesion is more a maceration of the epithelium than a true erosion, but sometimes diagnosis can only be made by the coexistence of other syphilitic lesions.

6. *Mercurial stomatitis* may cause erosions or diphtheroid patches, which may be mistaken for mucous patches. They usually occur behind the last molar tooth and on the sides of the tongue, rarely on the palate or gums. Diagnosis may be made by the presence of the other signs of mercurial stomatitis, salivation, fœtid breath, red and spongy gums, and by improvement when mercury is left off.

7. *Dental ulcers* may simulate mucous patches, but will be recognised by always corresponding to a broken or uneven tooth. However, a mucous patch on the tongue may become irritated and ulcerated by a broken tooth.

8. *Exfoliating marginate glossitis* simulates a syphilide of the tongue, and was for a long time thought to be a circinate syphilide. It is characterized by a fine grayish-white border of adherent epithelial accumulation in the form of segments of circles, which change their position from day to day. It is a benign lesion of unknown origin.

9. *Vincent's angina* is an ulcero-membranous or diphtheroid form of angina affecting the tonsils and pharynx, which

may extend to the palate and tongue. It begins with febrile symptoms, usually subsides in eight to fifteen days, and is caused by fusiform bacilli, associated with spirilla. According to Vincent, it is common in anæmic, syphilitic, and tuberculous subjects, and may secondarily infect syphilitic ulcerations of the throat. It is cured in a few days by the local application of tincture of iodine, and is not affected by mercury or iodides—two points which serve to diagnose it from syphilis.

Treatment.—Secondary syphilides of the mouth and throat require local as well as specific treatment; the lesions will not yield to mercury alone. Mucous patches and ulcerations should be cauterized with chromic acid (40 grains to the ounce). Fournier recommends acid nitrate of mercury or solid nitrate of silver. The liquid caustics should be applied with a wooden match, and *not* by means of wool wrapped round the end of a probe, as this may become detached and cause spasm of the glottis. Fournier records a fatal case in which this occurred.

The hygiene of the mouth should be carefully attended to, and smoking should be abstained from while lesions are present. Mouth-washes containing chlorate of potash and borax are useful, and gargles containing perchloride of mercury. In severe cases the author has obtained good results with a gargle of chlorine water.

Internally, a mixture of iodide of potassium and chlorate of potash (5 grains to the ounce of each) is useful in cases where there are many mucous patches, especially if these are ulcerated. Mercurial treatment should, of course, be continued. Recurrent erosions of the tongue frequently occur later than the third year of the disease, and are very resistant to treatment. Fournier recommends calomel injections for such cases.

2. Tertiary Syphilis.

The Lips.—Certain tertiary affections of the lips, although not very common, require special mention.

Tuberculo-crustate Syphilides of the lip are characterized by their tendency to frequent relapses. They are

generally circinate, and may be of considerable extent, especially on the upper lip. They occur sometimes with syphilides of the nose, cheeks, or chin. They are often hypertrophic, from association with gummatous infiltration of the subjacent tissues, sometimes causing considerable increase in size of the lip and disfigurement. These lesions may be mistaken for lupus, and in doubtful cases the therapeutic test should be applied.

Diffuse Hypertrophic Syphiloma consists in a general boggy infiltration of the whole of one lip, generally the lower. The skin is usually unaltered, but sometimes deep red in colour. The mucous membrane is swollen, and sometimes mammillated. This lesion may coexist with other syphilides, and especially with sclerosing glossitis.

Sclerosing Gumma.—This is a rare lesion, consisting in a hard, circumscribed gumma situated in the substance of the lip. It is important as regards diagnosis, as it may be mistaken for cancer; but the lymphatic glands are not enlarged. An ulcerating gumma may simulate hard chancre of the lip, but differs in the absence of glandular enlargement.

The Tongue.—Tertiary syphilis may affect the tongue in the form of localized gummata, or as a diffuse sclerosis, the latter being the more common condition.

Sclerosing Glossitis.—This causes an indurated, lobulated, or mammillated condition of the tongue, chiefly affecting the dorsum. The lobulation is produced by cicatricial contraction of fibrous tissue, in the same way as in the cirrhotic liver. The fissures between the lobules form an anastomotic network which is very characteristic, and this fissured and mammillated condition is not found in an equal degree in any other disease of the tongue. The mucous membrane is deep red in some places and pale in others, smooth, tense, or depapillated. Later on it may become white in places, owing to interstitial atrophy of the mucous membrane.

The process first causes enlargement of the tongue, which in some cases may attain a considerable size and project from the mouth (syphilitic macroglossia), but in the later stages the tongue shrinks from cicatricial contraction. It is always

chronic in evolution and liable to recurrent erosions of the surface, especially at the sides of the tongue, from the irritation of food, alcohol, tobacco, etc. 'Sooner or later every sclerosing glossitis becomes complicated by erosions, exulcerations, or even true ulcerations' (Fournier).

Gummatous Glossitis.—The gummatous infiltration may affect the mucous membrane or the parenchyma of the tongue, or both together. It forms single or multiple nodosities of various sizes, situated chiefly on the dorsum and sides of the tongue. The deep gummata occur in the muscular tissue, and may be lateral or median. They undergo the usual changes of gummata: softening, ulceration, and cicatricial repair. They generally form a projection on the tongue, sometimes of considerable size. The ulcer formed by the softened gumma is usually of oval form, and sometimes irregular, deep, and sharply cut out, with a thickened everted border and a yellowish adherent core. It may heal without treatment, having a depressed scar, or may remain for a long time as a chronic ulcer. Gummata and sclerosing glossitis may coexist, in the same way as gummata and syphilitic fibrosis of other organs. In some cases the ulcerated gumma becomes phagedenic.

The *symptoms* of tertiary syphilis of the tongue are remarkable by their benign character, unless the tongue becomes eroded or ulcerated. In this case there is pain on mastication and on any movement of the tongue; but the neuralgic pains which occur in cancer are absent in syphilitic glossitis. As a rule there is no glandular enlargement.

Diagnosis.—This has to be made from primary chancre, tuberculous ulceration, leucoplasia, and epithelioma. Chancre is generally easily distinguished by the presence of adenitis and by the characters mentioned on p. 60.

Tuberculous ulceration is more superficial than the gummatous ulcer; it is less excavated, and has thinner and more ragged borders. It is also more painful, and may occur on the under surface of the tongue, where gummatous ulcers never occur. Finally, the tubercle bacillus may be found in the lesion. There is, however, a rare form, described by

Fournier as 'gummatous tuberculosis' of the tongue, which may simulate syphilis. But this forms a cold abscess instead of the core of the syphilitic ulcer; also it does not react to iodides.

Leucoplasia resembles sclerosing glossitis in affecting the dorsal surface of the tongue, and in being frequently complicated by erosions and fissures. It differs in its pearly-white colour and by exfoliating in large lamellæ. When white patches occur in sclerosing glossitis, they are due to fibrosis of the mucous membrane, and are not exfoliating. Moreover, they have not the pearly-white appearance of leucoplasia (see also p. 132).

Epithelioma.—The diagnosis between syphilis of the tongue and epithelioma is most important, owing to the question of operative interference. Some cases diagnosed as cancer have been cured by antisyphilitic treatment. However, an epithelioma may develop on the site of a chronic syphilitic ulcer. The chief points of difference are: (1) Epithelioma is more circumscribed, forming a vegetating tumour of cartilaginous hardness with everted borders, generally situated on the side of the tongue; (2) it bleeds easily when irritated; (3) the saliva and breath are very fœtid; (4) there is early immobility of the tongue and difficulty in protruding it; (5) there is more pain, especially of a neuralgic character; (6) the glands soon become affected; (7) the age of the patient is usually between fifty and seventy; (8) it may occur on the under surface of the tongue; (9) it is often preceded by leucoplasia, which may be found on the tongue or inside the cheeks. In all doubtful cases a histological examination should be made.

Treatment.—The hygiene of the mouth should be carefully attended to, and spicy foods, alcohol, and tobacco avoided. Fournier recommends emollient mouth-washes of marsh-mallow, which are less irritating than alum or chlorate of potash. Erosions and ulcers should be touched with tincture of iodine or chromic acid (40 grains to the ounce).

Intensive general treatment is indicated by injection or inunction, combined with iodides internally. Fournier advises calomel injections in the dose of 5 centigrammes weekly. This

is the most powerful of all the preparations of mercury, and, according to Fournier, is the remedy *par excellence* for the tongue. As in all cases of buccal syphilis, it is a good plan to give chlorate of potash with the iodide internally. It is also advisable in cases of ulceration to try and obtain healing of the ulcer by the internal administration of this mixture, combined with local treatment, before beginning the mercurial treatment; or if the ulceration occurs during the course of mercurial treatment, to suspend this for a time, and resume it in a more energetic form after the ulcers are healed by the above method.

Gummata of the tongue quickly yield to specific treatment, but in advanced cases, and in sclerotic glossitis, little effect can be expected.

The Palate.—The hard and soft palate are *par excellence* the seats of election for tertiary syphilis.

The *hard palate* may be the seat of ulcerative gummatous syphilides, isolated gummata, or more often gummatous periostitis with necrosis and perforation.

The *soft palate* may be affected by gummatous syphilides, isolated gummata, or, more commonly, general gummatous infiltration.

A dry tubercular syphilide may also occur on either hard or soft palate, but is rare.

Ulcerative Gummatous Syphilides.—These consist of round or irregular ulcers, varying in depth and size, with a yellowish or gray base, and generally surrounded by a red areola. When multiple, they often assume a circinate form. Functional symptoms may be absent. When neglected and irritated, they persist for a long time without tendency to spontaneous repair. Under treatment they heal rapidly, but are liable to recur, either *in situ* or in adjacent parts. These lesions not only affect the anterior surface of the soft palate, but also occur on the posterior surface, where they can only be seen by rhinoscopic examination. This explains the occurrence of a certain number of throat affections in syphilis, which persist without any apparent lesion visible by direct examination.

Diffuse Gummatous Infiltration of the Soft Palate.—During the period of infiltration the soft palate is red, hard, thickened, and immobile. The process is insidious in development, and functional symptoms are slight. Ulceration is generally extensive, and sometimes causes perforation or mutilation. Perforation may be single or multiple, and when single is usually at the junction of the hard and soft palate; or the palate may be divided into two parts by a median ulceration; occasionally it is completely destroyed. Perforation causes the voice to become nasal and fluids to regurgitate through the nose. Under treatment the infiltration disappears and ulceration heals, leaving a white cicatrix. If perforation has occurred, various deformities may be produced, and the soft palate may be reduced to a fibrous membrane or a meshwork of fibres. In severe cases, coexisting with ulceration of the pharynx and base of the tongue, atresia of the fauces or velo-pharyngeal ankylosis may be produced.

Diagnosis.—Tertiary ulceration of the soft palate has to be diagnosed from tuberculous ulceration. The tuberculous ulcer is usually shallower, more limited in extent, with more ragged and less sharply-cut borders, and with a redder and more granular base than the gummatous ulcer. Tuberculous nodules may sometimes be seen near the ulcer, but they are more often absent. The submaxillary and anterior cervical glands are usually affected in tubercle, but rarely in gumma. Tubercle causes more pain and functional trouble, and a tuberculous ulcer rarely perforates. Moreover, tuberculous ulceration of the palate is usually associated with pulmonary or laryngeal tuberculosis. The tubercle bacillus may be found in the lesion, but is often absent. Inoculation of the guinea-pig may be used as a final test, but the therapeutic test with iodide of potassium is more valuable, and should be tried in every doubtful case.

The Tonsils.—Gummatous ulceration of the tonsils is generally unilateral, and is sometimes complicated by acute angina, with inflammatory and febrile symptoms. The glands are not affected unless this inflammatory condition is superadded. After cicatrization of the ulcer, the tonsil has a lobulated appearance.

Diagnosis must be made from chancre, cancer, tubercle, and lacunar ulcerative tonsillitis. *Chancre* differs by the characters mentioned previously (p. 61), and especially by the secondary glandular affection. *Cancer* is usually harder, of slower evolution, and generally accompanied by pain in the ear; it forms a vegetating growth, and not a deeply-cut ulcer like the gumma. Glandular infection occurs early in cancer. *Tubercle* of the tonsil is generally secondary to laryngeal or pulmonary tuberculosis, and the ulceration differs from gummatous ulceration in the characters mentioned above. *Ulcero-membranous tonsillitis* may simulate gummatous ulceration in some cases. Lacunar *ulcerative tonsillitis* is characterized by gray ulceration covered with caseous matter, which is easily removed, leaving a red, fungating surface with clean borders. The tonsil is not infiltrated, and the pillars are intact.

The Pharynx.—Tertiary syphilis of the pharynx is less common than of the palate or the tongue. It may be mucous or submucous, diffuse or circumscribed. Tertiary ulceration usually affects the posterior wall, and is often serpiginous. The gummatous ulcer is a typical, deep, circular, crateriform, sharply-cut ulcer with deep red, infiltrated borders and a dirty yellow base. Functional symptoms are usually slight, but in confluent lesions involving the pillars of the fauces there is considerable pain and dysphagia.

Naso-pharyngeal Ulceration may only be visible by posterior rhinoscopy, or may be seen by pushing up the soft palate with the handle of a spoon. Such cases, if not diagnosed, may give rise to much trouble, and lead to ulcerative destruction of the Eustachian tubes, causing deafness. The ulceration may extend to the nasal fossæ, causing necrosis of bone and 'tertiary ozæna.'

Deep pharyngeal gummata may attain a considerable size, and cause dyspnœa or dysphagia by pressure on the larynx or œsophagus.

Tertiary syphilis may affect the pharynx, palate, and tongue simultaneously. It may also become phagedenic, causing extensive destruction of the pharynx and nasal fossæ, and may extend to the larynx and œsophagus. Necrosis of bone may

result, sometimes of an extensive character. Fournier mentions an extreme case in which the mouth, nose, and pharynx formed a single cavity, and the turbinals, nasal bones, vomer, and nasal processes of the superior maxillæ came away as sequestra; the hard palate was destroyed, and the necrosis extended to the lachrymal, molar, ethmoid, and sphenoid; finally, the basilar process of the occipital bone dropped into the pharynx and nearly asphyxiated the patient.

Other complications which may occasionally occur are hæmorrhage from extension to the carotid arteries; caries of the vertebræ, causing 'syphilitic Pott's disease' (Chapter X.); and extension to the bones of the skull and meninges.

The combination of simultaneous lesions in the pharynx, soft palate, pillars of the fauces, and base of the tongue, may give rise, during cicatrization, to *guttural atresia*. The greater the destruction of the pharynx, the greater the risk of consecutive cicatrization. In a case of Ricord's the pillars of the fauces were united to the base of the tongue, causing much difficulty in deglutition. Sometimes the fauces are united by a diaphragm, perforated by a small hole.

In some cases the soft palate becomes united to the posterior wall of the pharynx (palato-pharyngeal ankylosis), dividing the cavity of the pharynx into two parts, the upper communicating with the nasal fossæ and the lower with the mouth. As a rule there is a median hole connecting the two, but this may be absent. This separation of the nasal fossæ from the pharynx renders respiration by the mouth a necessity, and causes dryness of the throat, loss of taste and smell, deafness, and intense earache.

Diagnosis.—Tertiary syphilis of the pharynx requires diagnosis from *lupus*. This differs from syphilitic ulcer in the following points: (1) It is of much slower progress; (2) it generally coexists with nasal or buccal lupus; (3) the borders of the ulcer are red and infiltrated, and gradually fade into the healthy tissue; (4) there is less loss of substance, and the ulcer is superficial and covered with red fungosities which may contain 'apple-jelly' lupus nodules. Finally, it does not react to antisyphilitic treatment. The diagnosis is more difficult in

heredo-syphilis of the throat, and when lupus occurs in a syphilitic subject, forming a kind of hybrid lesion.

Treatment.—In tertiary syphilis of the throat iodides form the main treatment, and have a remarkable therapeutic effect. Fournier recommends 1 to 2 drachms daily. Mercurial treatment is best suspended till ulceration has healed, and resumed afterwards. In early malignant tertiary syphilis, however, Fournier advises injections of calomel.

Locally, the mouth and pharynx should be disinfected with gargles of peroxide of hydrogen or chlorine water. Moure recommends the following gargle: Iodine, iodide of potassium, tincture of opium, and glycerine. The ulcers may be touched with tincture of iodine or insufflated with heated calomel (p. 96). Strong caustics, such as nitrate of silver, acid nitrate of mercury, etc., should be avoided, as they may add to the destruction effect.

If there is perforation of the soft palate, it may be healed with nitrate of silver if of small extent; if larger, an obturator should be worn, and the nitrate of silver treatment added. The physiological rest obtained by the obturator, by restoring the voice and preventing the irritation of the nasal fossæ by regurgitation of food, will tend to promote healing. A large perforation of the soft palate may be closed later on by staphylorrhaphy. Operative interference for adhesions and contractions is usually unsuccessful, and the formation of fresh adhesions may make matters worse. Hence it is not advisable to perform such operations unless there is rapidly-increasing deafness, constant earache, or much nasal stenosis.

Leucoplasia.

Most authorities agree that syphilis plays some part in the etiology of leucoplasia, and Fournier, Kaposi, Landouzy, Gaucher, Barthélemy, and others, regard all leucoplasias as of syphilitic origin, but *parasyphilitic* in nature.

The disease has received various names: buccal psoriasis, leucoplakia, lingual ichthyosis, leucoma, and 'smoker's patches.' More recently Besnier has given it the name of

leucokeratosis, as being more descriptive than the other terms. Leucoplasia is not peculiar to the buccal cavity, but also occurs on the vulva, anus, and prepuce, and in the larynx as pachydermia.

The lesion consists in bluish-white, pearly-white, or grayish-white patches, due to thickening of the mucous membrane. The patches may be thin, resembling a bluish varnish, or may be thick and parchmenty, and slightly raised above the mucous membrane. There is often submucous infiltration. The surface is usually smooth, but sometimes rough, and may become parquetted by movement; sometimes it is marked by ridges or horny acuminations. The shape of the patches may be rounded or polygonal, reticular, arborescent or stellate, or in the form of bands, or in sheets, which may cover the dorsum of the tongue like a carapace.

The lesions usually affect the dorsum, and sometimes the sides of the tongue; rarely the under surface. They also occur inside the cheeks and lower lip, but are rare on the palate or floor of the mouth. Inside the cheeks they form a commissural triangle. Desquamation may be slight or lamelliform, but seldom denudes the dermis. The surrounding mucous membrane is generally infiltrated and thickened, and the veins under the tongue are often varicose.

As the lesion progresses the surface of the tongue may become traversed by ramifying furrows, due to diminished resistance of the elastic tissue and muscle of the dermis, which becomes folded, owing to increase in its extent. These folds are liable to ulceration and erosion, especially on the edges of the tongue. When the disease has lasted some time, the mucous membrane is traversed by cicatricial bands, consecutive to ulceration, or to a sclerosis occurring in the evolution of the leucokeratosis, causing the surface to become mammillated, the nodosities so formed being soft or indurated in various degrees. In less marked cases the thickened epithelium covers only the filiform papillæ and their intervals, giving rise to a pearly-white or bluish-gray appearance.

On the vulva the patches have the same characters, and may cause contraction of the vulvar orifice (*kraurosis vulvæ*).

Leucoplasia sometimes evolves in successive crops, sometimes insensibly. Lamellar desquamation occurs at an advanced period of the disease. Erosions, fissures, ulcerations, cicatricial contractions, partial atrophies, and sclerosis, follow the evolution of the disease in an irregular way, without any definite order of sequence. The duration of leucoplasia is unlimited; it may end fatally in two years, or may be cured in a short time in benign cases. In most cases it persists during life, and often cuts it short by epitheliomatous transformation. This is especially liable to occur in cases with a rough papillomatous surface. The frequency of an epitheliomatous termination has, however, been exaggerated by former writers. Barthélemy found it 13 per cent. only.

Morbid Anatomy.—The pathological process consists in hyperkeratosis of the epithelium and embryonic infiltration of the dermis, ending in sclerosis. The infiltration, according to Kaposi, Schwimmer, and Leloir, commences around the vessels, which appear to be the point of origin. According to Leloir, the sclerosis is more marked in syphilitic leucoplasia, and is accompanied by endarteritis obliterans. This process of sclerosing dermatitis differentiates leucoplasia from true psoriasis.

Etiology.—The question arises whether leucoplasia is to be regarded as a morbid entity or as a symptomatic expression of various pathological processes. Another question is whether it can arise apart from the influence of syphilis.

Bénard's statement that 'leucokeratosis appears to be in certain cases absolutely independent of syphilis, and to develop in subjects who are evidently free from it,' is taking a very narrow view of the subject of syphilis. Many persons are 'apparently' free from syphilis, but no one can be said to be 'evidently' so. Tabes, for instance, may develop in a subject who has no evident signs of syphilis, but it is nevertheless accepted as of syphilitic origin.

With regard to the other alleged causes of leucoplasia, the chief of these are nicotinism and 'arthritism.' But in neither of these is there any distinctive pathognomonic characteristic. Smoker's patches usually occur in a triangular form inside the

commissures of the cheeks, but Besnier has shown that identical patches occur in glass-blowers. Moreover, smoker's patches have no relation to the intensity of the cause; they may occur in moderate smokers, and be absent in those who smoke excessively. Again, the existence of an 'arthritic' leucoplasia is purely hypothetical, and there are no characters which define it.

Syphilis appears to be the only well-established cause of leucoplasia, and it is admitted that the other forms of the 'idiopathic leucoplasias' have no characters to differentiate them with certainty. The therapeutic test does not apply in this case, as it does not exclude a parasyphilitic origin. Moreover, cases have been recorded of leucoplasia which reacted to anti-syphilitic treatment.

An argument in favour of the syphilitic origin of leucoplasia is the close resemblance which this sometimes has to tertiary syphilitic glossitis, both in appearance and in evolution. Fournier describes a superficial or lamellar form of sclerosing glossitis limited to the lingual dermis, as well as the more common generalized form causing mammillation of the tongue. This lamellar form bears a close analogy to leucoplasia, in which there is also sclerosis of the lingual dermis. The lesions in both cases occupy the same situation, progress in the same way, and are subject to the same complications. The chief objective difference, mentioned by Fournier, is the absence of desquamation in the white patches of sclerosing glossitis; but this desquamation is also said to be inconstant in the different forms of leucoplasia. Moreover, the two affections are said to be frequently blended and to combine their lesions in different forms. The only important difference between leucoplasia and sclerosing glossitis appears to be the presence of hyperkeratosis as an essential factor in the former.

The most recent investigations on leucoplasia are by Trapenard, who comes to the conclusion (1) that leucoplasia is always of syphilitic origin, and due to an embryonic connective-tissue formation caused by endo-periarteritis; (2) that it differs from other syphilitic lesions by the presence of

epidermic globes. He therefore regards leucoplasia as a syphilitic lesion, ready to become epitheliomatous under the influence of some irritant. Trapenard found evidence of syphilis in 92 per cent. of the cases he collected, and considered that *syphilis ignota*, or hereditary syphilis, would account for the rest. Landouzy also regards some cases as being due to the hereditary disease.

The evidence seems to point conclusively to the syphilitic or parasyphilitic origin of leucoplasia; that in some cases it is due to the hereditary disease; and that other factors, such as tobacco, are of secondary importance, and only act as accessory causes.

Another point worthy of consideration is the possible relation of *lichen planus* to leucoplasia. The lesions of lichen planus, when they occur on the mucous membrane of the mouth and tongue, may bear a remarkable resemblance to leucoplasia, and, according to Perrin, buccal lichen planus is capable of provoking leucoplasia, even in the parchmenty form. It may also be mentioned that lichen planus in general has by some been attributed to a syphilitic origin. This idea is, no doubt, in the present state of our knowledge, of a hypothetical and speculative nature; but it is more than possible that certain dermatoses of hitherto unknown or obscure etiology may trace their origin to syphilis, or at any rate to a syphilitic ancestry.

Treatment.—The first treatment for all kinds of leucoplasia consists in careful attention to the hygiene of the mouth and teeth, and in avoidance of tobacco, alcohol, or any spicy food which may irritate the lesions. Local caustics have been recommended, such as nitrate of silver, acid nitrate of mercury, lactic acid, bicyanide of mercury, etc. But these only act by the substitution of an irritable cicatrix for a comparatively indolent lesion. Moreover, they may provoke further irritation, increasing the tendency to epitheliomatous transformation. For these reasons local treatment by caustics would appear to be contra-indicated. Specific treatment usually fails, except in early cases. Iodides appear to have little or no effect, and also mercury in ordinary doses. Mercury may be tried in

the form of injections of calomel (1-grain doses), and some successful results from this treatment have been reported. Levy Bing recommends injections of gray oil.

With regard to the *epitheliomatous transformation* of leucoplasia, Fournier has observed this 97 times out of 324 cases, so that cancerous degeneration, although frequent, is not inevitable. Levy Bing regards leucoplasia as a connecting-link between syphilis and cancer, and points out that cancer is likely to result if the same causes persist which provoked the leucoplasia, such as tobacco, carious teeth, alcohol, etc. He, however, considers syphilis as a *sina quâ non* in the etiology of leucoplasia.

As soon as there is any appearance of epitheliomatous transformation in a patch of leucoplasia, this should be removed by excision when possible, with care to obtain union of the edges. Besnier points out that 'every method of surgical ablation which does not immediately render the surface exempt from suppuration and contaminations of all kinds is fatal to success, and should be rejected.'

II. The Œsophagus, Stomach, Intestine, and Rectum.

The Œsophagus.—In 1860 West reported a case of syphilitic stricture of the œsophagus in a girl of twenty-one, who had suffered for some time from severe syphilitic eruptions of the skin and throat. Treatment by mercury and iodide only gave temporary relief, and the patient died of inanition. At the autopsy 'the upper portion of the œsophagus for about 4 inches was much dilated, its mucous membrane thickened, and marked by spots having the appearance of recent cicatrices. At this distance from the upper end it was suddenly constricted, and terminated in a narrow canal, which would barely admit a No. 4 catheter. This constricted portion, which was about 2½ inches in length, was formed by the thickening of the mucous membrane and by fibrous deposit in the form of bands and bridles, having very much the appearance of an old stricture of the urethra. Below this track the œsophagus continued perfectly healthy to its termination in the stomach.'

Similar cases have also been described by Virchow, Wilks,

and others. They appear due to gummatous formation in the submucous tissue followed by ulceration, and contraction of the resulting fibrous-tissue formation, leading to stricture. Syphilis of the œsophagus, however, is very rare compared with that of the pharynx.

The Stomach.—Syphilis of the stomach is probably less rare than is generally supposed. Several remarkable cases simulating gastric ulcer, with repeated hæmatemesis, etc., which yielded rapidly to antisyphilitic treatment after the ordinary measures failed, have been recorded by Trousseau, Fournier, and Dieulafoy.

Morbid Anatomy. — The lesions consist in gummatous or sclero-gummatous infiltrations of the walls of the stomach, usually on the posterior wall and along the lesser curvature. They may be single or multiple, and are generally circular or oval, but sometimes irregular. They vary in size considerably, but the average size appears to be about that of a shilling.

The lesions go through the same stages of infiltration, ulceration, and cicatrization as gummatous lesions of the skin. The *ulcer* is usually single, more or less deeply excavated, circular, and with sharply-cut borders; sometimes there is only an erosion of the mucous membrane. The deeper ulcers may cause hæmorrhage by perforation of a vessel, but perforation of the peritoneum is rare. Apart from concomitant signs of syphilis, there is therefore little to distinguish the syphilitic ulcer from common round ulcer of the stomach.

Symptomatology.—Gastric syphilis presents itself under three chief forms: (1) Chronic gastritis; (2) round ulcer; (3) a form resembling gastric cancer.

1. The first form is characterized by dyspeptic symptoms: constant epigastric pain with exacerbations after food; later on, repeated vomiting with inability to retain food, and consequent wasting.

2. In the second form of gastric syphilis the manifestations simulate those of round ulcer of the stomach. The chief symptoms are pain extending from the ensiform cartilage to the spine, and hæmatemesis. In some cases hæmorrhage is repeated almost daily. The blood is usually red in colour,

owing to being immediately vomited after hæmorrhage has taken place; less commonly it is dark coloured and clotted. In rare cases hæmatemesis has been absent when ulcers have been found post-mortem.

3. The third form of gastric syphilis simulates cancer of the stomach. In addition to pain and gastric intolerance, a hard tumour can be felt in the stomach, sometimes in the pyloric region. Such cases are usually diagnosed as cancer, and have sometimes led to unnecessary operative procedures. When a gummatous mass is situated at the pylorus, signs of pyloric stenosis are produced. Fournier concludes that 'syphilis is capable of producing gastric tumours which, by the symptoms which result from them, by the reaction which they exert on the organism (weakness, often considerable emaciation, cachexia), and lastly by the evolution which they affect, may absolutely simulate cancer of this organ.'

Hayem has recently drawn attention to the subject of gastric syphilis, with a report on four cases. In the first case the patient was seized with profuse hæmatemesis, which disappeared under treatment by enemata of large doses of iodide of potassium; syphilis was suspected because the patient had recently been treated for syphilitic orchitis. In the second case, a man of thirty-three, the symptoms consisted in gastric disorder, wasting, and pain, which was attributed to gall-stones. A hard tumour the size of a small orange was felt near the pylorus. Both the tumour and the symptoms disappeared under antisyphilitic treatment. In the third case, a man aged forty-three, there was vomiting and wasting, but no hæmatemesis; no definite tumour was felt, but there was a diffuse thickening in the region of the gall-bladder. Stenosis of hepatic origin was diagnosed, and gastro-enterostomy performed. The patient died, and the growth was found to be syphilitic, containing small gummata. The fourth case concerned a man of sixty, suffering from slow digestion, and occasionally profuse vomiting. No tumour was felt, but stenosis was diagnosed and pylorectomy performed; the lesion was found to be syphilitic and not malignant. The patient was reported in good health more than a year later.

Diagnosis.—In the absence of other signs of syphilis diagnosis may be difficult, and may depend chiefly on the failure of the usual methods of treatment for gastritis and gastric ulcer. It is also necessary to bear in mind that hæmatemesis does not always indicate a lesion of the stomach, but may be caused by disease of the liver. Goldstein has recorded a case of fatal hæmatemesis, in which the liver was found affected with tertiary syphilis, and no lesion was found in the stomach.

There is, therefore, no special sign of syphilis of the stomach, and the main point in diagnosis is to keep in mind the possibility of gastric syphilis, especially in cases which simulate cancer. How many cases of round ulcer of the stomach are due to syphilis is impossible to determine, but Engel puts the figure at 10 per cent. It is possible that heredo-parasyphilis is a factor in the etiology of common gastric ulcer.

Treatment. — Fournier recommends mixed treatment by mercury and iodides, and states that these remedies are usually tolerated by the stomach in cases of gastric syphilis. Iodide (30 to 60 grains daily) should be given very diluted, and, if there is gastric intolerance, by means of enemata. Mercury is best administered either by inunction or injections. The diet should at first be the same as for ordinary gastritis or gastric ulcer. In cases of pyloric stenosis of obscure origin antisyphilitic treatment should be tried.

The Intestine.—Syphilis of the intestine, although comparatively uncommon, is probably unrecognised in many cases, and mistaken for some other affection. Galliard has described miliary gummata, ulcerating gummatous infiltrations, cicatrices, stenosis, and perforation of the intestine. The lesions are more common in the small than in the large intestine.

The *symptoms* of intestinal syphilis present nothing characteristic, and consist chiefly in chronic diarrhœa, a variable degree of abdominal pain, and sometimes dysenteric or hæmorrhagic motions, accompanied by gradual wasting and increasing cachexia. The *diagnosis* therefore depends on the coexistence of other syphilitic manifestations, the resistance to the usual remedies, and the beneficial effect of antisyphilitic treatment. The *treatment* is the same as for gastric syphilis.

Hayem and Tissier have reported a case of multiple ulcerations of the intestine in a woman of thirty-two, the subject of late secondary syphilides. The patient was suffering from profuse diarrhœa, and died in a typhoid state, in spite of energetic mercurial treatment. At the autopsy ulcerations were found in the cæcum, ascending and transverse colon. The ulcers were circular or oval in shape, with indurated borders and a red areola. These observers conclude (1) that in this case the ulcerations of the intestine could certainly not be imputed to tuberculosis, typhoid fever, or dysentery, and that, by exclusion, considering the existence of cutaneous lesions of an undoubtedly syphilitic nature, they must rationally be attributed to syphilis; (2) that the typhoid symptoms presented by the patient were certainly derived from the ulcerative lesions of the intestine, and that, consequently, 'along with the essential syphilitic *typhose* of Fournier there is a symptomatic syphilitic typhose due to ulcerative lesions of the intestine, the prognosis of which is even more grave, since death may result from it.'

'It therefore appears to result from the above observation that syphilis may cause ulcerative enteritis at the time when it is still manifested by secondary lesions; and that this enteritis may give rise to an assemblage of typhoid phenomena, constituting secondary typhose' (Fournier).

In connection with the subject of intestinal syphilis, it must be borne in mind that intestinal tuberculosis may coexist with syphilis.

Syphilis and Appendicitis.—Gaucher has recently drawn attention to the possible syphilitic origin of appendicitis (Société de Dermatologie et Syphiligraphie, April, 1904). Out of thirty-two cases of appendicitis, he found antecedent syphilis twenty-nine times (eight cases of acquired syphilis and twenty-one hereditary). Gaucher therefore believes that appendicitis may be 'a quaternary or late manifestation of syphilitic infection, or a *parasyphilitic* affection, derived more often from hereditary than from acquired syphilis.' Edmond Fournier also draws attention to the frequency of appendicitis in heredo-syphilitics. He has observed, in twelve families, sixteen cases

of appendicitis in children or young subjects affected with hereditary syphilis. Professor Fournier, without going so far as Gaucher, regards heredo-syphilis as likely to constitute a favourable soil for the development of appendicitis.

The Rectum.—Syphilis may affect the rectum in the form of ulceration, gummata, or contractile fibrous tissue. The ulcerative form is limited to the lowest part of the bowel, and is generally an extension from ulceration at the anus. Circumscribed gummata of the rectum are rare, but cases have been recorded by Zeissl and others.

Infiltrating Sclerosis. — This is the most common form of rectal syphilis, and the one which leads to stricture. Fournier terms it *anorectal syphiloma.* It consists in an infiltration of fibroplastic tissue in the submucous coat, extending gradually throughout the walls of the rectum and anus. This process is limited to the lowest part of the rectum just above the sphincter, and gives rise to stricture by the gradual contraction of the ring of fibrous tissue. This fibroid induration forms without ulceration of the mucous membrane, and in its early stages gives rise to little inconvenience. Later on, ulceration of the mucous membrane may take place and lead to abscess and fistula.

Syphilitic stricture of the rectum is more common in females than in males. In its early stages it is amenable to anti-syphilitic treatment; but patients seldom apply for relief till the stricture is far advanced. In such cases it should be divided posteriorly, and kept dilated by the passage of bougies, lubricated with mercurial ointment. Syphilitic stricture differs from malignant disease in being limited to the last 3 inches of the gut, and in its smooth surface. Dysenteric ulceration sometimes occurs in the rectum, but seldom gives rise to stricture (Cornil).

The Anus.—Syphilides are common around the anus, perineum, and intergluteal furrow, in the form of papulo-erosive syphilides and condylomata. The latter are especially common in women, in association with large condylomatous placards about the vulva.

Erosive syphilides at the margin of the anus often form

radiating fissures, which are especially painful during defæcation. They must be distinguished from non-syphilitic fissures, which are due to local irritation and neglect of cleanliness, possibly sometimes to sodomy. Fournier mentions a case in which a person was accused of a criminal assault on a child because the latter presented anal fissures, which were considered as evidence of venereal contamination.

Chancre of the anus is described with the extragenital chancres on p. 68.

III. The Liver.

Syphilitic lesions of the liver include (1) diffuse interstitial hepatitis, (2) circumscribed gummata, (3) amyloid disease, (4) acute yellow atrophy.

Interstitial Hepatitis. — This consists in a diffuse cell infiltration, originating round the walls of the small vessels, which are affected with syphilitic endo-periarteritis. Adami has shown that this infiltration occurs not only along the interlobular portal vessels, but also extends between the liver cells, constituting *pericellular fibrosis*. This small-celled infiltration develops into fibrous tissue, leading to cirrhosis of the liver, which may be diffuse or circumscribed.

By the contraction of the bands of newly-formed fibrous tissue the liver becomes lobulated and nodular on the surface; and this lobulation, in the case of the typical syphilitic liver, is coarser than the 'hobnail' appearance which is usually associated with alcoholic cirrhosis. This lobulation gives the edge of the liver an irregular border, which can be often felt below the ribs during life. However, this distinction must not be pushed too far, for it is probable that syphilis is an important factor in the production of the ordinary, or so-called alcoholic, form of cirrhosis. As Byrom Bramwell remarks, 'Why is it that one man who drinks gets cirrhosis of the liver, while another man who drinks does not? It is not improbable, I think, that in some cases (what proportion, whether large or small, I have no means of determining) the explanation is to be found in the fact that the man who gets cirrhosis of the liver has had syphilis.' In other words, syphilis renders

the connective and vascular tissues of the liver more vulnerable to other exciting causes. The same explanation probably applies to gout and cirrhosis of the kidney. Rolleston says there is reason to believe that parasyphilitic multilobular cirrhosis may occur in adults, but is difficult to recognise. Hermanides regards cirrhosis of the liver as parasyphilitic.

Gummata.—These are frequently found in the liver, usually associated with more or less interstitial hepatitis. They vary in size from that of a pea to that of a walnut, and consist of three zones—(1) a central zone of yellow caseous matter; (2) a middle zone of fibrous tissue; (3) an outer zone of condensed hepatic tissue, which is penetrated by fibrous-tissue extensions from the middle zone. The caseous matter is often absorbed, and the gumma is replaced by a condensed mass of fibrous tissue, which, if situated in the periphery of the liver, causes puckering of the surface.

In old-standing syphilitic disease of the liver there is usually perihepatitis, often with adhesions to the diaphragm, kidneys, and transverse colon. Rolleston figures a case of gumma of the liver which perforated the diaphragm and extended into the lungs. Secondary infection of a gumma may cause an abscess, and Newbolt has reported a case which gave rise to empyema.

Symptoms.—The symptoms of syphilitic cirrhosis may be the same as in cases of 'ordinary cirrhosis'—viz., jaundice, diarrhœa, epistaxis and other hæmorrhages, vomiting, and sometimes ascites. Lancereaux reports cases of ascites in tertiary syphilis which were cured by iodide of potassium, tapping, and the application of mercurial ointment to the abdomen. Jaundice is not common in tertiary syphilis of the liver, but may be caused by a gumma or cicatrix obstructing the portal fissure.

Diagnosis.—Hepatic syphilis is often overlooked and mistaken for alcoholic cirrhosis or malignant disease. Jaundice and ascites are more common in malignant disease than in hepatic syphilis, and gummata are of slower growth than malignant growths. In rare cases syphilis may cause enlargement of the liver, with chronic jaundice and splenic enlargement, but

the course is more rapid than in hypertrophic biliary cirrhosis. Tropical hepatitis may be associated with syphilis of the liver. In all doubtful cases the therapeutic test should be applied.

Syphilitic Malignant Jaundice (Icterus Gravis).—Jaundice sometimes occurs in the course of secondary syphilis, with the appearance and symptoms of ordinary catarrhal jaundice. This has been attributed to pressure on the bile-ducts by enlarged glands in the portal fissure. But in rare cases this jaundice assumes a rapidly malignant form, identical with that of *acute yellow atrophy* of the liver, and manifested by diffuse hæmorrhages, epistaxis, hæmatemesis, purpura, hæmaturia, subdelirium, convulsions, and coma. Such cases are nearly always fatal, and the post-mortem changes consist in atrophy of the liver and cellular necrosis of the hepatic cells. The pathogeny of these cases is obscure, and it is impossible to say whether the action of the syphilitic virus on the liver is aggravated by secondary microbic infection, or whether the condition is one of ordinary catarrhal jaundice which is aggravated by syphilis. Fournier suggests that it may be a parasyphilitic phenomenon. In any case it is not influenced by antisyphilitic treatment.

Rolleston regards the jaundice as due to general syphilitic hepatitis, resulting in pericellular infiltration, which, when excessive, runs on to acute yellow atrophy.

Lardaceous Disease.—This is a parasyphilitic affection, and is often combined with gummata of the liver. Syphilis is responsible for more cases of lardaceous disease now that suppuration has been diminished by antiseptic surgery.

IV. The Pancreas and Salivary Glands.

The *pancreas* is affected more often in hereditary syphilis than in the acquired disease, but in both cases interstitial perivascular fibrosis and gummata have been described. The relation of syphilitic pancreatitis to diabetes is described in Chapter XI.

With regard to the *salivary glands*, not much is known, probably because they are less often examined than the other

organs. Lancereaux described a case in which there was fatty degeneration of the submaxillary gland, with thickening of the interlobular septa, in a patient who had syphilitic lesions in other organs. Fournier also reported a case of swelling of the sublingual gland in a syphilitic patient, which disappeared under the influence of iodide of potassium. Neumann has published six cases of syphilis of the salivary glands, five affecting the parotid and one the sublingual gland. All these cases occurred in the secondary period in feeble, anæmic subjects. According to Neumann, syphilis may affect the salivary glands in the form of sclerosis or gummata. Syphilitic parotitis differs from mumps in its slow course, greater hardness, and in being usually unilateral.

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CHAPTER VIII

THE RESPIRATORY SYSTEM

The Nose.

THE initial lesion of syphilis may occur in the nostrils or in the nasal cavity, and has been described with the extragenital chancres (p. 62).

Secondary Syphilis may affect the nasal cavity with erythema and papular rhinitis, which are concomitant with the cutaneous eruptions. Mucous patches have been described, but are rare. The symptoms consist in coryza, with a certain amount of irritation due to the formation of pustules, scabs, and fissures.

Tertiary Syphilis frequently affects the nose in the form of gummata, ulceration and necrosis, with resulting scars and adhesions.

Gummata may be circumscribed or diffuse, and have a tendency to break down and ulcerate rapidly. They may occur on the septum, or on the inferior turbinate body. A gumma of the turbinate body resembles, at first sight, simple turgescence, but differs from this in not collapsing after the application of cocaine. Gumma of the septum generally forms an irregular infiltrating mass, blocking the nasal passage in parts. This must be distinguished from spurs or deviation of the septum. Occasionally a circumscribed gumma of the septum is seen, which must not be mistaken for a chronic abscess or for a sarcoma. Sarcoma is softer, generally pedunculated, and bleeds easily. In doubtful cases the therapeutic test with iodide of potassium will clear up the diagnosis.

Ulceration and Necrosis.—The periods of maximum intensity of ulceration and necrosis are from the first to the

third and from the eighth to the fourteenth years after infection. The gummatous infiltration may be in the submucous tissue or in the periosteum, and the result is the same in each case. The septum is most commonly affected, and may be perforated, with extension of the gummatous infiltration to the opposite side of the nasal cavity. A typical punched-out ulcer is seldom observed, because the ulceration becomes hidden with granulations, through which bare bone can be felt with a probe.

The same process may attack the turbinal body, or the floor and roof of the nose. There is a discharge of blood-stained pus with shreds of necrotic tissue, which later on forms large crusts with an offensive odour. The patient is at first conscious of the odour, but later on the sense of smell becomes abolished. At this period the general health suffers from the chronic septic poisoning. The septum is soon perforated, and granulations spring up around the hole, more or less concealing it. Sometimes large fibrous polypi develop on the septum or turbinal body, forming hard red masses devoid of epithelium, and hence differing from ordinary polypi.

Necrosis often occurs in spite of treatment, and any structure within the nose may be partially or completely destroyed. The vomer is generally the first to suffer; then the cartilage of the septum, the nasal bones, and lastly the turbinals, Necrosis of the floor of the nose leads to perforation of the hard palate, and necrosis of the roof of the nose may cause cerebral complications by extension of the septic process to the meninges.

Scars and Adhesions.—The nose may be considerably deformed both internally and externally by contractions developed during healing. There may, however, be much destruction within, but little deformity externally; and the vomer with part of the cartilage of the septum may be destroyed without causing external change.

The same is true in destruction of the turbinals and ethmoid bone; but if the vomer and the nasal bones are both destroyed, there is depression of the bridge, giving rise to the well-known 'saddle-back' nose. This is, however, more common in here-

ditary syphilis. Another common deformity is depression of the anterior part of the nose, caused by destruction of the cartilage and part of the bony septum. A third deformity is the 'bull-dog' nose,' caused by a combination of the above two processes. In this, the vomer, septum, and nasal bones are destroyed, so that the nose is sunk into the face. Lastly, the cartilaginous alæ may be destroyed, giving rise to various degrees of deformity and contractions, and sometimes to closure of the nostrils.

Complications.—These intranasal processes may, by extension to the Eustachian tube, cause catarrhal or purulent otitis, and also deafness from obstruction of the tube. Suppuration may also occur in the accessory sinuses of the nose, the walls of which may become involved in the necrosis.

Diagnosis.—In the earlier stages diagnosis has to be made from lupus and malignant disease, and in the later stages from ozæna.

In *lupus* the ulceration is more superficial and much slower in progress, and the overgrowth of tissue is in excess of the ulceration. There is also generally external lupus of the nose; the discharge is scanty, with less crusts, and free from odour.

In *malignant disease* the ulceration is on the surface of a new growth, which bleeds easily, and there are no crusts. The growth is friable and accompanied by pain. In doubtful cases the therapeutic test with iodide of potassium may be applied, or a small piece removed for examination.

In *ozæna* (confining the term to atrophic rhinitis) the odour is different and characteristic; granulations, ulceration, and necrosis are absent, and there is atrophy of the inferior turbinals. However, true ozæna may be a sequel of syphilis in cases where there has been much destruction of tissue and alteration in the mucous membrane. In these cases the ozæna is the result of syphilis, and not part of the syphilitic process.

Treatment.—Local treatment consists in the use of mercurial and alkaline douches, scraping the granulations, and insufflation of heated calomel (p. 96). Packing the nose with cyanide gauze is useful in keeping the mucous membrane clean and in checking the formation of scabs. Sequestra should be removed

when detached, and may require breaking up when too large to be removed in one piece.

The Naso-pharynx.

Primary and secondary syphilis of the naso-pharynx are rare. Primary chancres have been described as the result of the use of contaminated Eustachian catheters, etc. Tertiary syphilis of this region is usually associated with syphilis of the nose or pharynx, but occasionally the affection is confined to the naso-pharynx. In such cases the symptoms consist in pain at the back of the throat, deafness, tinnitus, and headache, with a blood-stained discharge from the nostrils. An ulcerated swelling may be seen in the naso-pharynx or on the posterior surface of the velum. When the velum is affected, it is much thickened and soon becomes perforated.

Felix Semon reports a case of tertiary syphilis of the naso-pharynx developing three months after a similar condition of the larynx and trachea had yielded to treatment.

The pharynx is dealt with in the chapter on the Alimentary System.

The Larynx.

Chancre of the epiglottis has been described with the extra-genital chancres (p. 60).

Secondary Syphilis.—The manifestations of secondary syphilitic laryngitis include erythema and mucous patches.

Erythema.—In the first stage there is often a bright red erythema, diffuse or localized to the region of the vocal cords. The erythema is punctiform, and often accompanies similar lesions of the skin and throat. Sometimes there are small erosions, due to partial or total desquamation of the epithelium. The secretion is increased in quantity and becomes viscous, accumulating on the vocal cords.

Mucous Patches.—These generally appear at the same time as roseola of the skin, and nearly always coexist with mucous patches in the mouth. They are usually situated on the lingual surface of the epiglottis, on the glosso-epiglottic folds, and on the vocal cords. They form gray, raised patches, with

a corrugated surface surrounded by a red inflammatory border. On the vocal cords they are almost diphtheroid in appearance, but have a clearly-defined red margin. Sometimes they form simple erosions. They may occur on one or both vocal cords, generally on the upper surface.

Œdema.—The mucous membrane surrounding the patches sometimes becomes swollen and œdematous, so as to cause stenosis of the glottis, with attacks of suffocation. The secondary inflammatory swelling nearly always affects the epiglottis and its folds, more rarely the ventricular bands or the subglottic region. These severe complications of the secondary period usually occur in patients who use the voice excessively, and are aggravated by the abuse of tobacco and alcohol. These accidents may also be due to violent cauterization.

Condylomata.—True condylomata are rare, but occasionally occur. Moure reported the case of a girl, aged six, in whom the anterior pillars of the fauces and the base of the epiglottis were covered with grayish-white papillary tumours, giving the mucous membrane the appearance of being covered with an irregular false membrane, or rather, a diffuse papilloma. These lesions are tenacious, and recur in spite of treatment.

Symptoms.—During the period of erythema the voice is little altered in tone, but is sometimes harsh and raucous. When mucous patches appear, the vocal change is more pronounced; dysphonia is common, or even aphonia, according to the seat and intensity of the lesion. If the patches are extralaryngeal, there may be slight pain on deglutition. In cases of œdema there is dysphagia, respiratory obstruction, and sometimes attacks of suffocation. A persistent catarrhal laryngitis should lead to the suspicion of syphilis as a possible cause.

Tertiary Syphilis.—Tertiary lesions generally appear from ten to twenty years after the chancre; but gummata have been reported by Mauriac and Felix Semon in the first year of the disease. Semon also describes cases of early malignant syphilis of the larynx in the first year.

Tertiary laryngitis also forms one of the manifestations of

heredo-syphilis, and Moure says he has seen children tracheotomized for a so-called croup, which was in reality a manifestation of heredo-syphilis.

The tertiary manifestations of laryngeal syphilis comprise gummata, ulcerations, and cicatricial contractions.

Gummata. — Circumscribed gummata have usually a smooth red surface, accompanied by surrounding inflammation, which defines them clearly. When they begin to soften, they present at different points small yellow projections, around which is produced the crateriform ulceration which characterizes them later. It is not uncommon to see a series of gummatous projections crowded together, giving the mucous membrane an irregular mammillated surface; these lesions are situated on a red infiltrated base, which is distinct from the rest of the normal mucous membrane.

The infiltrating gumma presents the appearance of a smooth red inflammatory swelling, causing distortion of the normal configuration.

These syphilides occur in order of frequency on the base of the tongue, the epiglottis, the ventricular bands, the aryepiglottic folds, the false vocal cords, and especially in the subepiglottic region. The lesion is generally unilateral, occupying one side of the epiglottis, which is folded on itself, deviated externally, and fixed by the infiltration. The affected part is only immobilized when there is at the same time inflammation of the crico-arytenoid articulation. It is not uncommon to see gummatous infiltration pass from one side to the other, and affect both sides of the larynx.

Ulceration.—This generally constitutes the second stage of the gummatous process, but the phase of infiltration may develop so rapidly that it may pass unnoticed. In these cases the patients are seen when the ulceration is already established. The ulceration is superficial at first, but rapidly extends in breadth and depth, extending to the submucous tissue, and finally to the cartilage, which first becomes ossified and then undergoes necrosis. According to the soil and the degree of infection of the patient, the process extends with variable rapidity, and the larynx becomes filled with red poly-

poid vegetations, at the same time that the edges of the ulcer become infiltrated, if specific treatment has not arrested the progress of the disease. The epiglottis may be perforated, ragged, or nearly destroyed. The interior of the larynx is deformed by loss of substance, and the ulcer assumes an irregular form with fringed borders. As a rule, the borders are projecting, and more or less sharply cut, sometimes detached by the ulcerating process, which extends deeply, causing crateriform ulceration.

At this period of the ulcerative process there may be extensive detachment of mucous membrane, which floats in the interior of the larynx, and causes suffocation if it is not removed with forceps. According as the ulcers follow a circumscribed or diffuse gumma, the ulceration becomes punched out and reaches the perichondrium or the cartilage, or extends to the neighbouring regions of the tongue and pharynx.

Perichondritis.—In some cases the perichondrium and the cartilages are affected primarily, the ulceration being secondary. In these cases there is rapid destruction of the framework of the larynx, with the production of necrotic ulcers and elimination of partially ossified and necrosed cartilage. In these forms of primary perichondritis the swelling is visible externally, and forms a carapace in front of the larynx, which is characteristic of thyroid perichondritis. The cartilage is painful to touch, and fistulous tracts may form both internally and externally.

Pseudo-polypoid Form.—In certain cases of syphilis diffuse pseudo-polypoid degeneration may affect the whole larynx. These lesions resemble diffuse papillomata, but the mammillations are more voluminous, more projecting, and redder. The posterior region and the ventricular bands are thickened and infiltrated, and present a pachydermatous appearance. This degeneration is almost a quaternary syphilitic manifestation, and only reacts partially to treatment. It is always necessary to employ the forceps and galvano-cautery in order to re-establish the permeability of the larynx, which is obstructed by the swelling of the mucous membrane and the infiltration beneath.

Felix Semon has recently reported a case in which these

papillomatous growths developed in a severe case of recurrent tertiary laryngeal syphilis, in which there had previously been recurrent ulceration of the epiglottis and fibroid thickening over the cords of the arytenoids. He describes the growths as 'a periodical sprouting of irregular pale excrescences, occasionally condylomatous, but more frequently papillomatous in shape, which arose sometimes more slowly, sometimes with almost incredible rapidity, from almost any part of the interior of the larynx, but most frequently from the vocal cords themselves, from the interarytenoid fold, and from the ventricular bands. After being in existence for variable lengths of time, they then always completely disappeared, sometimes spontaneously, sometimes under the influence of specific treatment, either gradually or quickly, just as they had made their appearance.' In this case it is interesting to note that there were no other signs of syphilis while the patient was under observation; so that, had not the previous state of the larynx been known, the diagnosis might have been difficult.

Stenosis of the Larynx.—The different changes described above may, after attaining a certain degree, leave permanent cicatrices, causing variable degrees of stenosis. Both vocal cords may be united by a membranous bridge, or there may be ankylosis of the arytenoids, resulting from an arthritis or from a cicatricial band. There may also be hyperplasia, or cicatricial contraction due to the elimination of cartilage, leading to laryngeal stenosis. Lastly, an annular stricture may be formed, with a narrow opening.

These changes can easily be seen with the laryngoscope. When there is a membranous bridge, a white membrane is seen during inspiration; this is grayer in colour than the cords, and generally occupies the anterior third of the larynx, forming a crescent with its concave border behind.

Paralysis.—The nerves of the larynx may be affected by paralysis of peripheral or central origin. The paralysis may affect the abductors or adductors of the cords, or the whole of the laryngeal muscles. The latter condition may be due to compression of both recurrent laryngeal nerves by glands or aneurism, or may be due to syphilitic lesions. Complete

laryngeal paralysis is, however, rare, apart from cancer of the œsophagus.

Of the different forms of paralysis, that of the abductors and unilateral paralysis of the recurrents are the most common in syphilis. Paralysis of the recurrent nerve may be due to a peripheral neuritis, to compression by peritracheal glands, or to aneurism of the aorta, innominate, or subclavian, which are themselves evidence of former syphilis.

Paralysis of cortical origin is very rare, and seldom occurs in syphilis. Risien Russel has recently shown that there is a cortical centre for the movements of the larynx, which is equal in both hemispheres; hence the rarity of paralysis of the larynx of cortical origin. Laryngeal paralysis is much more usually of bulbar origin. It is also one of the early signs of tabes dorsalis, in which paralysis of the abductors is the usual form.

Hughlings Jackson reported a case in which there was paralysis of the face, tongue, palate, and vocal cords on the [illegible] caused by syphilitic lesions affecting all the nerves on [illegible]

Symptomatology. [illegible]

Rapid suffocation may occur if a fragment of necrosed cartilage or a piece of detached mucous membrane falls into the air-passages; also if acute œdematous infiltration occurs.

The breath is rarely fœtid, and if this symptom occurs it is generally due to a necrotic focus in the nasal fossæ or lungs.

Spontaneous pain is generally absent, and pressure on the larynx almost painless. Deglutition is generally easy and painless, except when the inflammatory lesion occupies the epiglottis or the posterior part of the larynx. In this case it may be almost as acute as in tuberculous laryngitis, and cause trouble in nourishment. Liquids cause a burning sensation, with pain in the ears which renders alimentation difficult. The liquids also often regurgitate by the nose or get into the air-passages, provoking attacks of coughing. The sensibility of the back of the throat is lessened, contrary to what occurs in tuberculous cases, and hence laryngoscopic examination is easy.

Prognosis.—The prognosis of laryngeal syphilis should be guarded, as the disease is generally of long duration. The erythema and mucous patches may persist for months, with the raucous voice which accompanies them. However, as a rule, the secondary lesions disappear gradually under the influence of appropriate treatment. The paralysis only may remain permanent, and if in many cases the voice becomes nearly normal, it is not owing to restoration of the function of the paralyzed vocal cord, but to a compensatory action on the part of the opposite cord, which allows juxtaposition during phonation.

The duration of tertiary lesions depends on their form, date, and intensity. As a rule, if the patient comes for advice at first, when the infiltration or ulceration is of recent date, a cure may generally be obtained. But if the perichondrium or the cartilages are affected, the prognosis is less favourable. Affection of the crico-arytenoid articulations is very tenacious and liable to recurrence.

The termination of secondary syphilis of the larynx is in complete resolution without cicatrices. The tertiary lesions

leave no trace if treatment has been instituted early and sufficiently. On the other hand, in severe cases, with much destruction of tissue or cartilage, the disease ends in cicatrices or adhesions of variable degrees of severity.

Stenosis due to destructive ulceration is of grave prognosis. The dangers of suffocation may be avoided by tracheotomy, but the tube must be worn indefinitely. Death from hæmorrhage caused by deep ulceration has been reported, and fatal infection may result from gangrene of the larynx, trachea, or bronchi.

Diagnosis.—In the secondary period it is usually easy to diagnose syphilitic erythema or mucous patches, on account of the coexistence of lesions of the skin, throat, etc.

Gummata at the period of infiltration are easy to recognise by their appearance and their progressive course. At the ulcerative period tertiary lesions may be mistaken for tuberculous.

In *laryngeal tuberculosis* the cough, expectoration, and dysphagia are more pronounced than in syphilis. *Tubercle* has a preference for the posterior part of the larynx, especially the arytenoid region, and the lesions are more diffuse and irregular. There is anæmia of the mucous membrane of the vocal cords and deficient mobility in the early stages of tuberculous laryngitis, and there is more discoloration of the tissues. In syphilis the lesions are more limited, often confined to one half of the larynx, and have a preference for the ventricular bands, subglottic regions, and epiglottis. When the epiglottis is affected in syphilis, the base of the tongue and wall of the pharynx are almost always affected. Syphilis generally avoids the posterior region of the larynx.

Tuberculous ulceration differs from syphilitic in being more superficial and diffuse, and is more painful. The syphilitic ulceration is more localized, serpiginous, and crateriform, and makes more rapid progress than the tuberculous. The mode of formation also differs, the tuberculous ulcer starting in several spots, which coalesce; while the syphilitic ulcer commences in one spot, which extends in surface and in depth. In fact, the course of laryngeal syphilis is gradual, progres-

sive, and often rapid, while that of tuberculosis is slow, except in acute diffuse forms, and the ulceration is rarely localized to one part of the larynx. Syphilis extends and radiates from one spot.

Hybrid forms may occur in which signs of both syphilis and tuberculosis are present. The diagnosis may then be difficult, but these cases are rare. Finally, examination of the sputum for bacilli and the lungs for signs of pulmonary tuberculosis will aid in the diagnosis. Inoculation of the guinea-pig will also help to decide the question.

However, it must be borne in mind that laryngeal syphilis predisposes to tuberculosis, and, as Landouzy remarks, 'laryngeal syphilis, even when cured, has acquired the necessary qualifications for laryngeal tuberculosis, which may break out at any time.'

A gumma commencing to ulcerate may be mistaken for *cancer*. In both cases there is a red circumscribed swelling, occupying the epiglottis or one of the ventricular bands. In both cases the affected part is painless, but the course of the two affections is very different. Spontaneous pain radiating towards the nape of the neck or the back of the throat usually occurs in cancerous lesions. The occurrence of small hæmorrhages or of blood-stained expectoration is more suggestive of cancer than gumma. Also in malignant ulceration the breath is more fœtid. The progress of cancer is much more rapid than that of syphilis.

When a tumour is formed, the diagnosis is more easy, for the swelling of a cancer should not be confounded with a syphilitic fungous ulceration, in which the projection is less and the ulceration more extensive and serpiginous. The cancerous tumour bleeds easily, and is surrounded by a hard inflammatory zone of infiltration, which is not so marked in syphilis. In the malignant growth the corresponding vocal cord is often fixed early—an occurrence seldom observed in syphilis, except in arytenoid arthritis. If the tumour is extra-laryngeal, the special adenopathy will help in diagnosis.

Lastly, the appearance of perichondritis with the formation of a kind of laryngeal shield is a common occurrence in cancer.

When this sign appears in syphilis, there is such extensive disorganization in the larynx that the diagnosis is obvious. The diagnosis may be confirmed by microscopic examination.

In hybrid cases, which are rare, diagnosis is very difficult; but in these forms it is usual to see syphilitic lesions invading the base of the tongue and pharynx with serpiginous ulceration, combined with cancerous lesions consisting of red, indurated, infiltrating swellings with bleeding granulations, accompanied by hard, painful, adherent glands.

Lupus may attack the epiglottis and aryepiglottic folds, but is characterized more by fungating projections than by deep ulceration. The ulceration of lupus is more superficial, much slower in evolution than that of syphilis, and characterized by a granular appearance, due to the gray or yellowish projections of the lupus nodules. Cicatrization takes place at one part while the ulcer extends at another. Lupus of the larynx, moreover, seldom occurs without similar lesions in the oropharynx (p. 130).

Treatment.—In severe cases of laryngeal syphilis a thorough mercurial treatment is required, either by inunction or injections, combined with iodides internally. In administering iodides supervision is required if there is any tendency to stenosis, as the iodide is apt to cause œdema of the larynx and increase the obstruction.

Felix Semon reports a case of early malignant syphilis of the larynx which benefited by Zittmann's treatment (see Appendix). In this case mercury aggravated the condition.

Local Treatment.—Applications of nitrate of silver, 2 to 4 per cent., or iodine-iodide solution are useful:

Iodine	gr. i.
Iodide of potassium	gr. ii.
Laudanum	♏x.
Glycerine	ʒi.

In tertiary ulceration of the larynx the insufflation of sublimed calomel is one of the best methods. The apparatus used for this purpose consists of a glass tube with a bulb in the centre, one end of the tube being connected with an india-

rubber blower, the other end being drawn to a fine point. The calomel is placed in the bulb and heated by a small spirit-lamp, and as it sublimes is blown by the rubber bag on to the affected surface. In the case of the larynx a curved glass tube may be connected with the end of the main tube, and passed into the larynx.

Cicatrices after ulceration and membranous bridges are best treated by the galvano-cautery, after applying cocaine and adrenalin to the mucosa. Simple section is not always sufficient, and requires to be supplemented by slow and progressive dilatation.

The Trachea and Bronchi.

Trachea.—The trachea is occasionally attacked by tertiary syphilis, but such cases are rare. The parts of the trachea usually affected are the upper and lower extremities. Gummatous infiltration soon leads to deep circular ulceration, followed by perichondritis and necrosis of cartilage. The lesion generally perforates the trachea, and extends to the surrounding tissues and glands. If healing of these lesions takes place, the cicatricial contraction causes stenosis of the trachea.

Wilks reported a case in which a syphilitic ulcer of the trachea caused death by perforating the aorta. Beger reported a case which caused perforation of the œsophagus, leading to escape of food into the bronchi and fatal pneumonia.

The bronchi are more rarely affected, but Lancereaux and others have described cases of ulceration of the bronchi extending to the smallest ramifications. Kelly reported a case in which an ulcer, at the point of division of the right bronchus, caused fatal perforation of the pulmonary artery. Stenosis of the bronchi is rare, but several cases have been reported.

Symptoms.—The affection is generally far advanced before any definite symptoms are produced. Pain behind the sternum is said to be a marked sign, and later on attacks of dyspnœa and dry cough appear. When the ulceration is advanced, the sputum is purulent or blood-stained. During

the process of cicatrization dyspnœa becomes more pronounced, and may cause death by exhaustion or by pneumonia.

Diagnosis.—Dyspnœa occurring without signs in the lungs in a syphilitic patient suggests syphilis of the trachea, which can be distinguished from laryngeal syphilis by laryngoscopic examination. The prognosis is usually fatal.

Bronchi.—Catarrhal bronchitis may occur in the early secondary period along with the roseola, and is probably due to erythematous lesions of the mucous membrane. In the tertiary period *sclero-gummatous infiltration* is more common than isolated gummata. The bronchial lesion is often bilateral, and usually affects the commencement of the two main bronchi. Rolleston has reported two cases of stenosis of the main bronchi caused by sclero-gummatous syphilis.

Bronchial syphilis is usually associated with chronic interstitial syphilitic pneumonia (syphilitic phthisis), which may lead both to stricture and dilatation of the bronchial tubes.

The Lungs.

Syphilis may affect the lungs in the form of circumscribed gummata or interstitial fibrosis; but usually both processes occur together, as in the liver (sclero-gummatous syphilis).

Gummata.—These occur in the interstitial tissue of the lung in the form of gray or yellowish tumours, slightly irregular, and varying in size from a pea to a walnut. They are first firm and elastic in consistence, afterwards soft and caseous. They are generally surrounded by a zone of dense fibrous tissue. The gumma may be partially or completely absorbed, but is more often evacuated by the bronchi, leaving a cavity, which may afterwards become obliterated by cicatrization, causing puckered depressions on the surface of the lung. Many cicatrices found in the lungs post-mortem are probably due to syphilis and not to tubercle. They are commonly found in association with visceral syphilis of the liver and other organs.

A gumma situated near the surface of the lung may implicate the pleura, giving rise to fibrous adhesions and thickening of the pleura.

Fournier mentions five points of distinction between syphilitic

gumma and tubercle: (1) Tubercle involves the upper part of both lungs, gumma is generally limited to one lobe of one lung; (2) gummata are few in number compared with tubercles; (3) they are larger than tubercles, and never miliary in form; (4) the gumma is white or yellow, and never transparent like miliary tubercle; (5) the gumma is harder in consistence than tubercle, and does not break down altogether, owing to its fibrous capsule. Both tubercle and gumma are formed by small round cells, but the gumma is less rapid in development and more organized than tubercle, which has a greater tendency to caseate and break down. Gummata always develop in fibrosed tissue, while tubercles are often isolated in healthy tissue.

Interstitial Pneumonia (Syphilitic Phthisis).— This consists in a process of chronic interstitial fibrosis of certain portions of the lung, generally disseminated and of small extent. The process begins in a small-celled infiltration, which soon develops into vascular fibrous tissue, arranged around the interlobular vessels and smaller bronchi. The alveoli are compressed and the interalveolar septa thickened. The smaller bronchi become constricted by pressure in some places and dilated in others. This syphilitic fibrosis is probably identical with what has been otherwise named 'fibroid phthisis.'

In an autopsy made by the author at the Lock Hospital, on a woman of forty-six, there was found chronic interstitial pneumonia affecting the middle lobe and upper half of the lower lobe of the right lung, and most of the lower lobe of the left lung, together with a gumma in each lung, situated in the consolidated parts. In this patient there was also tertiary ulceration of the skin, perforation of the hard palate, interstitial hepatitis and perihepatitis, with scars of old gummata in the liver, and fatty degeneration of the heart secondary to syphilitic myocarditis.

Fournier, in 1873, reported a remarkable case of cure of syphilitic phthisis. A young woman was admitted to the Lourcine Hospital with syphilitic phagedena of the foot. She was apparently also in the last stage of consumption, and had signs of a large cavity at one apex. However, under mercurial inunction and iodide of potassium both the phage-

dena and the pulmonary lesion healed, and the patient regained her health.

Dieulafoy describes two forms of acute syphilitic pneumonia —(1) a form resembling tuberculous broncho-pneumonia, but differing in its more rapid progress and in being amenable to mercurial treatment; (2) a form of pulmonary gangrene.

According to Milian, a syphilitic soil, especially in early secondary syphilis, predisposes to pneumococcal infection. He has observed two cases of pneumococcal cerebro-spinal meningitis in the subjects of secondary syphilis, and thinks that secondary erosions of the mucous membranes furnish points of entry for the germs.

Symptoms and Diagnosis.—Pulmonary syphilis is insidious in its development, and may pass for some time unnoticed or remain latent. The symptoms consist at first in slight dyspnœa and cough, with little or no expectoration. The physical signs are not marked unless a superficial patch is developed, when signs of consolidation may be observed. Later on the dyspnœa and cough increase, and there may be abundant muco-purulent expectoration, with occasionally hæmoptysis. When the lesions are far advanced, the general condition and symptoms resemble ordinary phthisis, but are less rapid in progress. Fournier describes three degrees of syphilitic phthisis: (1) In the first the disease is latent, with no symptoms, and is not detected till after death. (2) In the second form there is some dyspnœa, but the general condition is unaltered; the physical signs are those of induration or cavitation. (3) The third form is severe, and presents the features of well-marked consumption. The prognosis depends on the extent of the lesions and their reaction to treatment. A remarkable tolerance to the disease is sometimes seen, which is in favour of syphilis rather than tuberculosis. Another point of distinction is the slower evolution in the case of syphilis.

Fournier concludes that—(1) tertiary syphilis can produce in the lungs lesions which, either locally or by reacting on the general symptoms, simulate pulmonary phthisis. (2) These lesions are often amenable to specific treatment. (3) When

a case of pulmonary lesion presents itself, it is important to ascertain if the lesion can be traced to syphilis. It is necessary to remember that syphilis is a possible cause of phthisis. (4) When syphilis is suspected to be the cause, specific mixed treatment should be prescribed, which has been known to give good results.

Lancereaux remarks that 'a certain degree of dulness, with tubular breathing, not preceded by febrile reaction, persisting, and limited to one of the lower lobes, or middle lobe, in a cachectic individual, in whom the apices of the lungs are intact and the liver diseased, constitutes a great presumption in favour of a pulmonary syphilitic affection. The sudden appearance of abundant expectoration, the limited extent of the lesion, especially to one side of the chest, are circumstances which also support the diagnosis of this affection.'

Syphilitic phthisis also differs from tuberculous in the usual absence of the hectic fever, night sweats, and diarrhœa. Examination of the sputum is also, of course, important. Although the presence of the tubercle bacillus does not absolutely negative syphilis, since both affections may coexist, the absence of tubercle bacilli in the sputum in an apparently phthisical subject is strongly suggestive of syphilis.

Treatment.—Syphilitic pulmonary disease is amenable to early treatment, even in cases of cachexia; but when left to its own evolution it is almost invariably fatal, from hæmoptysis, secondary infection, or cachexia. Energetic mercurial treatment is indicated, either by inunction or injection. Iodides are of less value.

When the pulmonary lesions have caused much destruction, a cavity is sometimes left, which persists indefinitely. This cavity is generally dry, and gives the usual signs on stethoscopic examination.

Syphilitic Pleurisy.—In the early secondary stage a benign and usually dry form of pleurisy has been described by Chantemesse. It is often associated with syphilitic synovitis, and sometimes with bronchitis. In the tertiary stage gummatous lesions of the pleura may occur in association with gummata of the lung.

Pleural effusion may also be due to neighbouring syphilitic lesions of the lung, vertebræ, pericardium, aorta, mediastinal glands, and even the liver.

Syphilis and Tuberculosis.

Syphilis and tuberculosis may be associated in the same subject: on the one hand, a tuberculous subject may contract syphilis; on the other hand, a syphilitic subject may develop tuberculosis. Gummata and tuberculous foci have been reported as occurring in the same lung. Syphilis, in fact, is a powerful *predisposing cause to tuberculosis*. Tuberculisation of a syphilitic subject may occur in one of two ways—directly or indirectly.

1. Direct tuberculisation may take place by bacillary inoculation of a syphilitic ulcer of the skin or mucous membrane. This form of infection is rare, owing to the inflammatory reaction and phagocytosis, but may occur in cases of ulcerating syphilides of slow evolution, especially in the *larynx*.

2. Indirect tuberculisation is more common, and is due to diminished resistance of the tissues to tuberculous invasion, caused by antecedent syphilis. Fournier remarks: 'I have already seen a number of young subjects, in whom syphilis had powerfully exerted its depressing influence, become tuberculous in the first months or the first years of infection. I even venture to state that, under these conditions, phthisis sometimes pursues a rapid course, and is soon fatal. Again, from my own personal experience, as well as from what has been said on this subject by the highest authorities, I do not hesitate to inscribe syphilis in the etiological chapter of pulmonary tuberculosis.'

According to Sergent, tuberculisation may occur in the early stages of syphilis, or later on, when syphilis appears to have died out. This is especially the case in syphilitic heredity, where a syphilitic soil, which is vulnerable to tubercle, may be transmitted by a syphilitic parent to the child. Then, after an attack of adenoids, bronchitis, enteritis, etc., the tubercle bacillus finds a suitable soil for germination,

and attacks the glands, joints, mucous membranes, or lungs. 'Thus, the non-syphilitic child of a syphilitic parent becomes scrofulous or tuberculous; the syphilisation of the father has prepared the soil for the tuberculisation of the child.'

Hence in many cases a so-called 'hereditary predisposition to consumption' may be really a hereditary syphilitic soil, which predisposes to tuberculosis. This can only be decided by inquiring into the history of the parents and grandparents —a method of procedure which is difficult to carry out, and also seldom thought of. In any case, it is obvious from the above considerations that the stock question, 'Is there consumption in the family?' can hardly be regarded as fulfilling the requirements of the case.

Sergent reports several cases of pulmonary tuberculosis in which he found syphilis present in one of the parents. He is of opinion that tubercle developing in syphilitic subjects is amenable to mercurial treatment, and that inverse cases, in which the tubercle precedes syphilitic infection, may also be improved, owing to the tendency of syphilis to cause cicatrization.

When tuberculosis develops in a subject with recent syphilis, it pursues a rapid course, and is usually fatal, especially when the subject is also alcoholic. On the other hand, tuberculosis attacking an old syphilitic is generally slow and benign in evolution, and the general health may remain good for a considerable time, in spite of signs of cavitation and abundant bacilli.

Pulmonary syphilis may also predispose to *cancer* of the lung, in the same way that leucoplasia, or tertiary syphilis of the tongue, predisposes to cancer of that organ.

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CHAPTER IX

THE GENITO-URINARY SYSTEM

The Male Organs of Generation.

The External Genital Organs.—Chancres of the penis and urethra have been described in Chapter IV.

Papulo-erosive syphilides or *mucous patches* occur on the balano-preputial furrow and inner side of the prepuce; papular syphilides and condylomata on the scrotum and penis. Syphilides occurring on the scrotum have a tendency to become eczematous, and when neglected may cause œdematous swelling of the scrotum and perineal raphe. Mucous syphilides of the glans or balano-preputial furrow may cause secondary balanitis and phimosis, and in neglected cases sloughing of the prepuce may occur.

Sometimes mucous syphilides undergo a process of secondary induration, forming what Fournier terms *pseudo-chancres*. These may be mistaken for primary chancres, and may possibly explain some reputed cases of reinfection, in which the diagnosis was based only on the presence of a supposed second chancre (*vide* p. 45). Such cases emphasize the fact that induration is not a special character of the chancre, but is characteristic of the syphilitic process, and is due in each case to dense perivascular infiltration. These pseudo-chancres differ from the chancre in the absence of concomitant enlargement of the inguinal glands.

Genital syphilides are very contagious, and apparently insignificant erosions may give rise to syphilitic contamination.

Diagnosis.—Syphilides of the external genitals have to be diagnosed from—(1) soft chancre, (2) abrasions, (3) lichen

planus, (4) psoriasis, (5) diabetides, (6) scabies, (7) herpes progenitalis, (8) circinate erosive balano-posthitis.

Soft Chancre. — This is distinguished by its punched-out circular appearance, with a red areola, and by its yellow, irregular base, discharging pus containing the bacillus of Ducrey.

Abrasions.—Simple abrasions often closely simulate erosive syphilides, but are usually more fissured and painful, with less rounded contours.

Lichen Planus.—This may occur on the penis and scrotum, and even on the glans as part of a general eruption. It presents the usual characters of lichen planus, and can hardly be mistaken for a syphilide (p. 81).

Psoriasis.—There is a clinical type of steatoid psoriasis which affects the genital organs, inguinal region, and scalp. The patches are paler, more greasy, and less squamous than those of ordinary psoriasis, and may be mistaken for papulo-squamous syphilides. The latter, however, are always associated with characteristic syphilides on the other parts of the body, and other signs of syphilis are usually present.

Diabetides.—These are small erosions of the balano-preputial furrow occurring in diabetic subjects. They differ from syphilides in being intensely pruritic and more inflammatory. Sugar is usually present in the urine. This affection should be borne in mind in middle-aged obese patients who present erosive lesions of the genital organs.

Scabies.—The penis and glans are common situations for scabies. As scabies is only contracted at night, the acarus being noctambulant, sexual connection is the usual cause of contagion, and the first lesions occur on the genital organs and hypogastrium. Scabies may thus be looked upon as a venereal disease. The lesions on the penis consist of a mixture of vesicles, pustules, and burrows, in which the acarus may be found. On the glans penis the lesions form circular, flat, red erosions, which may be mistaken for erosive syphilides. The latter are, however, rare on the glans itself. It must be remembered that scabies is the most common pruriginous affection of the penis.

Herpes Progenitalis.—This consists in an eruption of groups of ovoid vesicles, preceded by itching and smarting. The eruption occurs usually on the prepuce or in the balano-preputial furrow. The vesicles arise on an erythematous base, which afterwards forms a red areola for each vesicle. In a few days the vesicles rupture, leaving red erosions, which may be mistaken for syphilides, but differ from these in their clear polycyclic outline, caused by the coalescence of several vesicles. The affection is liable to frequent recurrences, and is a source of anxiety to persons who have exposed themselves to syphilitic contagion. Moreover, herpetic lesions on the penis may furnish points of entry for the syphilitic virus.

Circinate Erosive Balano-posthitis.—This is a special venereal affection caused by *spirilla* (Berdal and Bataille), affecting the balano-preputial furrow in men and the clitoris in women. It is characterized by the formation of superficial erosions, with a circinate whitish border formed by macerated epithelium. There is abundant suppuration, and spirilla can be found in the pus. It was formerly supposed to be of gonorrhœal origin, but is now known to be a morbid entity. The pus does not contain gonococci, and does not cause gonorrhœa when inoculated into the urethra; but when inoculated on the balano-preputial furrow of a healthy subject it reproduces the same lesion containing spirilla. The affection occurs chiefly in young subjects, and, like other forms of balanitis, is predisposed to by a long prepuce and retained smegma, causing fragility of the epithelium. The erosions vary in number, and may become confluent, but never extend to the urethra. The affection is of benign evolution, and undergoes spontaneous resolution.

It is easily diagnosed from mucous patches by the above characters. It differs from simple balanitis due to the decomposition of retained smegma by the presence of the circinate white margin of macerated epithelium, and from herpetic erosions by the smaller size of the segments of the polycyclic border.

Circinate erosive balano-posthitis is a lesion of no importance, and is cured by simple cleanliness. It is chiefly of

interest owing to the presence of spirilla, which might be mistaken for the *Spirochæta pallida.*

Some authors describe a *pustulo-ulcerative* form of balanitis of venereal origin caused by staphylococci. This would appear more likely to be a secondary inoculation of herpetic or other erosions than a distinct affection.

TERTIARY LESIONS.—*Gummata* of the penis are more common than is generally supposed, and when ulcerated are often mistaken for chancres. They are often situated in the same place as the former chancre.

Tertiary Chancriform Syphiloma.—This term is applied by Fournier to a small circumscribed gumma which becomes eroded on the surface, and simulates a hard chancre. This is another lesion which may explain some of the reported cases of second infection (p. 45). It usually appears after the third year of the disease, and is generally situated in the balano-preputial furrow; sometimes on the penis, prepuce, or scrotum. It differs from chancre—(1) in the absence of adenopathy; (2) in consisting of an erosion secondary to induration, whereas in the chancre the induration is secondary to the erosion.

Diffuse Hypertrophic Syphiloma.—This is a diffuse gummatous infiltration of certain parts of the penis, giving rise to various deformities of the organ.

Phagedena.—Gummatous ulceration of the penis sometimes becomes phagedenic; and, according to Fournier, most cases of phagedena of the penis are connected with tertiary syphilis, and not with chancres.

The Urethra.—Ulceration of the mucous membrane of the urethra can be seen by the endoscope in some cases of secondary syphilis. Gummata of the urethra are rare, and generally secondary to gumma of the glans. A rare form of cylindrical syphiloma of a segment of the urethra has been described, which may lead to stricture. Pericavernous gummata may also occur.

The Epididymis.—In the third or fourth month of secondary syphilis epididymitis may occur, usually unilateral. This differs from gonorrhœal epididymitis in being confined to the

upper part of the epididymis, whereas in gonorrhœa the lower part or whole of the organ is affected. Syphilitic epididymitis is also less acute, and often painless.

The Testicle.—Syphilitic orchitis occurs during the tertiary period of the disease, seldom before the third year. Like tertiary syphilis of other glandular organs, such as the liver, it may assume the form of interstitial fibrosis or circumscribed gummata.

Interstitial Orchitis.—This is a chronic interstitial fibrosis affecting the whole of the connective tissue of one or both testicles. The testicle is uniformly enlarged; the epididymis and cord are usually unaffected, but occasionally present nodular thickenings; the skin of the scrotum is unaltered, but there is usually effusion into the tunica vaginalis. The affection is painless and of insidious onset, and if left to its own evolution tends to fibrous atrophy of the testicle and consequent aspermia. If both testicles become atrophied, sterility and possibly impotence result.

On section, the tunica albuginea and fibrous septa are seen to be thickened, and the seminal tubules separated by newly-formed fibrous tissue. The tubules themselves are infiltrated with round cells, and the epithelial cells have undergone granulo-fatty degeneration.

Gummatous Orchitis.—This is only a more advanced degree of interstitial orchitis, with circumscribed gummata, which presents the usual anatomical characters of gummata in general. When situated under the tunica albuginea, the gummata may cause a nodular condition of the testicle, which can be felt by examination.

Diagnosis.—The following table shows the chief points in diagnosis between syphilis, cancer, and tuberculosis of the testicle.

Syphilis.	Tuberculosis.	Cancer.
1. Begins in the testicle.	Begins in the epididymis.	Begins in the testicle.
2. Slow evolution.	Slow evolution.	Rapid evolution.
3. Scrotum unaltered.	Scrotum involved when abscess forms.	Scrotum finally involved.

Syphilis.	Tuberculosis.	Cancer.
4. Suppuration and fistula rare.	Suppuration and fistula common.	Fungus testis common.
5. Feeling of weight and dragging.	Slight pain.	Pain severe and lancinating.
6. Swelling hard and uniform.	Irregular, and later on soft and nodular.	Soft and fluctuating.
7. Moderate size.	Moderate size.	Much enlargement.
8. Painless on pressure, and generally loss of testicular sensation.	More or less painful on pressure.	Painless on pressure.
9. Often affects both testicles.	Often affects both testicles.	Generally only one testicle affected.
10. Inguinal glands unaffected.	Inguinal glands usually unaffected.	Inguinal, iliac, and lumbar glands affected.
11. Spermatic cord seldom affected.	Spermatic cord usually affected.	Spermatic cord often affected.

The Bladder.—Syphilitic lesions of the bladder are apparently very rare, and only three genuine cases are on record, cases previously reported being probably tuberculous in nature. Margulies has reported two cases, one of which was diagnosed as cancer, but was cured by antisyphilitic treatment; in the other, ulceration was seen by the cystoscope, and this also healed under specific treatment. A similar case has been reported by Le Fur.

The Prostate.—Syphilis of the prostate is also rare, although, as Lancereaux remarks, 'among the numerous tumours situated in the prostate some may arise from syphilis.'

The Pelvis.—In 1902 Professor Fournier reported a remarkable case of *gummatous pelvic cellulitis* in a heredo-syphilitic man, aged thirty-four. This lesion, which formed a pelvic tumour obstructing the bladder and rectum, was diagnosed as an inoperable sarcoma by several leading surgeons. Fournier, on the strength of the patient's brother presenting ophthalmoscopic stigmata of heredo-syphilis, and a probable history of syphilis in the father, instituted antisyphilitic treatment by injections of benzoate of mercury and iodide internally. Under

this treatment the tumour entirely disappeared in the course of two months. The moral is to try antisyphilitic treatment in all cases of 'inoperable sarcoma.'

The Female Organs of Generation.

The Vulva.—Chancres and secondary syphilides of the vulva have been described in Chapters IV. and V. Mucous syphilides of the vulva have to be diagnosed from soft chancre, herpes, diabetides, and psoriasis.

Soft chancre usually occurs on the labia minora and fourchette; syphilitic chancre on the labia majora or about the clitoris.

Herpes is less common in women than in men, and affects the inner surface of the labia majora. It has the same characters as in the male.

Diabetes causes intense pruritus, erythema, and erosions affecting the labia majora (diabetides). These erosions are generally situated between the labia majora and minora, or on the inner surface of the former, in the form of red, irregular pruriginous patches, with little discharge and slow evolution. The intense itching is sufficient to diagnose them from mucous syphilides. However, mucous syphilides of the vulva may occur in a diabetic subject, and the diagnosis must then depend on the presence of other signs of syphilis.

Psoriasis may occur on the labia majora, but differs from papulo-squamous syphilides in the characters mentioned in Chapter V.

Hypertrophic Syphiloma of the Labia.—Apart from œdema or inflammatory swelling, there is a form of induration affecting the whole or part of one or both labia. This condition is probably due to subcutaneous and submucous plastic lymphangitis, and in its extreme form gives rise to the condition known as *elephantiasis* of the vulva (p. 93). The swelling is hard, painless, and does not pit on pressure.

Gummata.—The vulva is often affected by diffuse or circumscribed gummata and tertiary ulceration. The ulcerations may be single or multiple, and may affect all parts of the vulva and entrance to the vagina. They are generally irregular in form, and less characteristic in appearance than gummatous

ulcers in other situations; sometimes, however, they assume a circinate form. They are liable to become inflamed and painful from the irritation of vaginal discharges and neglect of cleanliness. Tertiary ulceration of the vulva often causes various mutilations and deformities; the labia majora may be enlarged and elephantiasic, and the labia minora may become rigid, twisted, or form irregular lumps. Phagedena is rare.

Diagnosis.—Tertiary syphilitic ulceration of the vulva has to be diagnosed from tuberculous ulceration and epithelioma. Tuberculous ulceration differs in the same characters which are mentioned on p. 94. A tertiary ulceration, accompanied by hypertrophic syphiloma of the vulva, might at first sight suggest epithelioma; but the absence of any true fungating tumour is easily made out, and, if necessary, the diagnosis can be settled by microscopic examination. A tertiary syphilitic ulceration may, however, be the starting-point of an epithelioma.

There is an ulcerated condition of the vulva which was called by the older writers *esthiomenus*. Fournier calls this 'phagedenic scrofula, or lupus of the genitals,' but Sabouraud regards it as a chronic ulceration due to vaginal discharges and want of cleanliness. Very probably esthiomenus corresponds to the condition found in old, broken-down prostitutes, in the causation of which tertiary syphilitic ulceration, chronic vaginal discharges, want of cleanliness, and perhaps tubercle, take part.

The Vagina.—Syphilitic lesions of the vagina are usually confined to the lower part, and are due to extension from lesions of the vulva. Sometimes a gumma forms in the recto-vaginal septum, and this may lead to the formation of a recto-vaginal fistula.

The Uterus.—The recent experimental inoculation of monkeys with syphilis, through the semen of a syphilitic subject, by Finger, show that an *intra-uterine chancre* is theoretically possible, although it is impossible to say how often this occurs. It is possible that this may explain certain cases which not infrequently occur where no chancre is discovered.

The *cervix uteri* may be affected by primary chancre, which often causes extensive induration. Ulcerative syphilides also

occur on the intravaginal portion of the cervix, in the form of yellowish-gray sharply-cut ulcers, often of a circinate form. These differ from common cervical erosions in not radiating from the external os and in the absence of pain.

Syphilitic Endometritis.—The body of the uterus may also be affected by tertiary ulceration, which gives rise to muco-purulent discharge and hæmorrhage. Some cases of chronic fungating endometritis which do not yield to curetting and other local measures are syphilitic in nature, and may be cured by antisyphilitic treatment.

Syphilitic Parenchymatous Metritis.—This is a form of perivascular and periglandular metritis which passes through two stages—(1) a hypertrophic stage, in which there is enlargement of the uterus, with pain and hæmorrhage; (2) an atrophic stage, in which the muscular tissue becomes atrophied, and the organ is reduced to a condition of fibrosis, with consequent atresia of the uterine cavity.

Metrorrhagia is an important symptom, and cases which at first sight appear to suggest uterine cancer should be given a trial with antisyphilitic remedies. It is possible that syphilitic metritis predisposes to cancer, in the same way as tertiary syphilis of the tongue. Barthélemy remarks that 'conceptional syphilis, even in its latent forms, strongly predisposes to cancer, not only of the genital organs, but also of the breasts.'

Gummatous Metritis.—Gummata have been found in the uterus at post-mortem examinations, and some cases diagnosed as uterine fibro-myomata have been known to disappear under antisyphilitic treatment. Uterine gummata differ from fibro-myomata in being usually more numerous, softer, and of smaller size. They differ anatomically in being surrounded by a fibrous zone, which sends prolongations into the surrounding tissue.

Barthélemy suggests that the uterus is liable to infection from a syphilitic fœtus; that 'we are therefore justified in assuming that uterine syphilis is more frequent than has hitherto been supposed, either by direct infection or by conceptional syphilisation.'

The Fallopian Tubes. — A condition of chronic fibroid **syphilitic salpingitis** has been described, causing general thickening of the walls and obliteration of the lumen. Bouchard and Lepine reported a case (1866) in which three gummata were found in each tube; there were also gummata in the liver and brain.

The Ovaries.—The ovary may be affected by fibrosis or by gummata, in the same way as the testicle; but, as the ovary is less accessible for purposes of diagnosis than the testicle, ovarian syphilis is not so often recognised. Lancereaux reports two cases, in one of which the ovary was fibrous and attached by adhesions to the Fallopian tube and surrounding parts; in the other case two swellings, the size of an egg, which were felt in the region of the ovaries disappeared under treatment with iodide of potassium. Lancereaux also gives a figure of a gummatous ovary.

The *symptoms* of syphilitic ovaritis are not distinctive, apart from other signs of syphilis. There may be pain and tenderness in the region of the ovary, but the chief sign is menorrhagia in the earlier stages, followed by intermittent metrorrhagia. The chief point is to bear in mind syphilis as a possible cause of ovarian disorders, and to give antisyphilitic treatment a trial.

The Peritoneum. — The peritoneum surrounding the uterus, tubes, and ovaries may be affected by fibro-gummatous peritonitis; and, according to Barthélemy, *pelvic peritonitis*, which is usually attributed to gonorrhœa, puerperal infection, cancer, or tubercle, is not infrequently due to syphilis.

Local pelvic peritonitis may also be secondary to lesions of the bone. The pelvis may be affected by tertiary syphilis, either in the form of rarefying osteitis, or exostosis. The latter may form swellings of sufficient size to cause dystocia. Barthélemy mentions a case in which there were eleven osseous gummata on the bones of the pelvis, two of which formed a palpable tumour, which was diagnosed as osteosarcoma, but which disappeared under mixed treatment by mercury and iodide.

The Mammary Gland.—Syphilis may affect the mammary gland in the form of interstitial mastitis or gummata. The former condition is comparatively uncommon, but cases of chronic mammary tumour which disappeared under iodide of potassium have been reported (Lancereaux). Gummata of the breast are more common, but rare compared with gummata in other situations.

Diagnosis.—Syphilitic mastitis has to be diagnosed from cancer, tuberculosis, and adenoma. *Cancer* is distinguished by the early appearance of pain; later on by implication of the skin and retraction of the nipple. The axillary glands are affected at an early period in cancer, but not at all in syphilitic mastitis. *Adenoma* is usually more lobulated and more freely movable than syphilitic mastitis, but may be difficult to distinguish in the absence of other signs of syphilis.

A gumma of the breast, after involving the skin, breaks down into a typical crateriform gummatous ulcer. It differs from tuberculous ulceration in the characters previously mentioned, and from cancer by the absence of any true fungating tumour, and from both by the absence of axillary adenitis.

It is quite possible that syphilitic mastitis may be the starting-point for the development of a cancerous growth of the mamma, in the same way that tertiary syphilitic glossitis predisposes to cancer of the tongue. It is also possible that some cures of cancer of the breast by early operation have been cases of syphilitic mastitis. On this point Lancereaux remarks that 'the exact knowledge of these morbid manifestations would permit, more often, perhaps than would be supposed, the substitution of a certain and always inoffensive treatment for an operation which is not free from danger.' It would therefore appear advisable to give all cases of doubtful mammary tumour a trial with mercurial and iodide treatment.

The Kidney.

Tertiary syphilis of the kidney was described by Virchow in 1858, but secondary syphilitic nephritis has only been studied more recently, chiefly by Fournier, Darier, Dieulafoy,

Balzer, Barthélemy, Chauffard, Lancereaux, Mauriac, Neisser, Rénon, and others.

Syphilitic nephritis may be divided into two groups, according to the date of appearance in the evolution of syphilis: (1) *Early nephritis*, appearing in the secondary period, and resembling the nephritis of acute infectious diseases; (2) *late nephritis*, appearing in the tertiary period, in the form of chronic atrophic, sclerous, or gummatous lesions.

This division is useful as applying to the majority of cases, but is not absolute; for cases of early nephritis may develop slowly, become chronic, and end in renal lesions similar to those observed in the tertiary period. On the other hand, in the same way that cutaneous eruptions of the secondary type are sometimes observed several years after infection, cases of acute or subacute nephritis may occur at an advanced period of the disease. Moreover, acute outbreaks may occur in the course of chronic nephritis

'The kidney may be attacked by the syphilitic infection, as it may be by other infections. The symptomatology of nephritis of infectious origin varies little, according to the different causes. All these nephrites closely resemble each other, and we must not look for any special physiognomy, for they only differ from one another by gradations in symptoms, and even in lesions. The mature or softened gumma of the kidney is a lesion which is usually easy to recognise; but in the cicatricial stage it is difficult to distinguish from a sclerous nephritis. The differences between the varieties of acute or chronic nephritis are equally difficult to determine on account of the acute phases which occur in the evolution of chronic nephritis. Thus, after a nephritis, apparently parenchymatous, of short duration one may find old lesions in the kidneys resulting from a long latent period' (Balzer).

Cases of nephritis occurring in secondary syphilis have been attributed to the effect of *mercury* by some writers, but it has been repeatedly shown that nephritis occurs in syphilitics who have taken no mercury. Moreover, *mercurial albuminuria* corresponds to the periods during which the drug is administered; for instance, it may appear after each inunction of mercury

and disappear during the intervals. Also, the amount of albumin caused by mercury is much less than in syphilitic nephritis. The harmful effect of mercury on the kidney is doubted by Fournier, Neumann, and other high authorities, and it appears that workers in mercury do not suffer much from renal diseases. It is true that experiments on animals have shown that mercury may cause acute interstitial changes ending in fibrosis; but the recent researches of Gravagna have demonstrated that mercury *in therapeutic* doses causes no damage to the kidneys, and that granular and fatty degeneration of the renal epithelium is only caused by excessive doses.

It is probable that mercury causes only a slight renal irritation with transient albuminuria, which has no permanent effect on the kidney.

Frequency of Renal Syphilis.—With regard to the *frequency* of renal syphilis, the results of statistics differ considerably, owing partly to the fact that many cases are unrecognised or cause no obvious symptoms during a course of mercurial treatment for other syphilitic lesions, and also to the fact that many cases of nephritis of syphilitic origin are attributed to other causes. Karvonen states that from 25 to 30 per cent. of autopsies show renal lesions attributable to syphilis, apart from amyloid disease, and that about 25 per cent. of syphilitics die with lesions of the kidneys.

On this point Balzer remarks as follows: 'The domain of syphilis is always extending at the expense of that of other causes of renal affections, designated by most authors under the name of common causes. As Darier has justly said, it is not surprising that the kidneys, the principal emanatory organs of the body, which eliminate so many poisons and toxins, should be sometimes damaged by syphilis; it is rather more astonishing that they are so often immune in the course of this affection. Rénon states that syphilis creates a strong predisposition to nephritis. Fournier, on account of the frequency of unrecognised syphilis, thinks that many cases of nephritis of obscure etiology are in reality caused by syphilis. To sum up, apart from renal gummata, there exist a small number of nephrites the nature of which may be clearly affirmed as

syphilitic by their symptomatology, the results of treatment, or by pathological anatomy. In many other cases the syphilitic etiology is still probable for the same reasons. Lastly, there remains an important class of doubtful cases in which the symptomatology presents nothing special, the etiology is obscure, and the treatment is without certain effect, for it must be remembered that specific treatment may be useful even in non-syphilitic nephritis. Here prudence is the rule in forming conclusions, but the physician should nevertheless bear syphilis in mind. Failure of specific treatment is not enough to negative syphilis, for sclerous nephritis of the tertiary period forms part of the important group of syphilitic scleroses which are rebellious to treatment and are found in nearly all organs, such as the tongue, rectum, liver, nervous system, etc. In fact, among these doubtful cases, *many may be more rationally attributed to syphilis than to any other cause.*'

Other causes, such as tubercle, alcohol, malaria, and exposure to cold, may act at the same time as syphilis, and cause the latter to become localized in the kidneys. In such cases it may be difficult to determine the part played by syphilis in the causation of the nephritis; but, as Balzer remarks, 'One must not be too sceptical with regard to syphilis. It is quite as rational to accept the etiological rôle of an infection so profound and tenacious, so prolific in visceral localizations, as that of ordinary causes of nephritis, which are so often vague in their presence and in their mode of action.' According to Balzer, many cases of nephritis of obscure origin may be regarded as *parasyphilitic.*

Secondary Syphilitic Nephritis.—This is a diffuse acute or subacute nephritis, usually occurring in the first year of syphilis, sometimes in the first few months. The kidney is of the type of *large white kidney*, and the lesions may be parenchymatous or interstitial. In one type epithelial changes predominate, and are due to the intensity of the toxic agent. The convoluted and straight tubules are filled with coagulated albuminous urine; the epithelial cells are granular and vacuolated (protoplasmic cytolysis), and there is a slight degree of endo-periarteritis.

In another type the lesions are chiefly interstitial, and consist in thickening of Bowman's capsules, endarteritis of the arterioles, atrophy of the tubules, and interstitial fibrosis. The cells of the atrophied tubules undergo fatty degeneration.

In most cases the two types of lesions—parenchymatous and interstitial—are associated, constituting diffuse nephritis. Some forms of subacute syphilitic nephritis develop into the type of chronic interstitial nephritis; others pass on to tertiary syphilitic nephritis.

Symptomatology.—The characteristic feature is the appearance of nephritis at the same time as secondary syphilides. Chauffard has remarked in some cases a coincidence of extensive cutaneous lesions with nephritis, and also a recrudescence of albuminuria at each successive skin eruption. There may be prodromal symptoms of malaise and a slight rise of temperature, but the first symptom is often œdema. This has a tendency to become generalized, and spreads rapidly from the eyelids to the lower limbs and scrotum. Pulmonary œdema and pleural or peritoneal effusion may supervene.

The *urine* is scanty, and there may be complete anuria. The main characteristic is the large quantity of albumin, which is greater in syphilitic than in any other form of nephritis. From 15 to 30 grammes of albumin per litre of urine is a common amount, and over 100 grammes has been reported. The urine contains epithelial, blood, or granular casts. The urea is diminished. Renal impermeability is often considerable, as shown by the methylene-blue test (Chauffard).

Syphilitic nephritis is often complicated by gastro-intestinal symptoms, such as vomiting and diarrhœa. Headache, delirium, and eye symptoms are uncommon. The evolution of the disease is rapid, and death may occur from gastro-intestinal uræmia, general dropsy and dyspnœa, anuria, and profuse diarrhœa; more rarely from coma. On the other hand, mercury, if given early, causes a rapid diminution in the albuminuria and dropsy, and may cure the nephritis. Sometimes the cure is incomplete, and the albumin may

persist without other symptoms; at other times improvement alternates with relapse.

Diagnosis.—This depends chiefly on the presence of other signs of secondary syphilis and on the effects of antisyphilitic treatment. In the absence of definite evidence of syphilis, the presence of a considerable amount of albumin with intense œdema, the absence of acute infectious disease, and the continuance of the albuminuria in spite of the usual treatment and diet, justifies the assumption of syphilis as the cause of the nephritis, and the administration of mercurial treatment.

Tertiary Renal Syphilis.—The kidney may be affected by tertiary syphilis in three ways—(1) by gummata; (2) by interstitial nephritis; (3) by amyloid disease.

Gummata of the kidney are comparatively uncommon. They are usually associated with gummata of the liver and spleen. According to Virchow and Cornil, they sometimes suppurate.

Nephritis is usually interstitial, and leads to cirrhosis of the kidney (granular atrophic kidney). The pathological condition consists in fibrous glomerulitis, fibrous infiltration of the kidney substance, and degeneration of the tubules. The characteristic feature is the frequent presence of *endarteritis obliterans*. Sometimes one kidney only is affected.

Amyloid Disease.—This is one of the most common results of renal syphilis, and may occur apart from any suppurating lesion of the bones, etc. It generally affects the liver, spleen, and intestine, as well as the kidney. Amyloid degeneration is found in the arterioles and sometimes in the walls of the kidney tubules; it is recognised on section by the usual reagents (tincture of iodine, etc.).

Mixed lesions are often found on post-mortem examination, consisting in sclero-gummatous changes combined with amyloid degeneration. Miliary gummata occur enclosed in a meshwork of fibrous tissue. In such cases the left ventricle is usually hypertrophied.

Symptomatology.—This is the same as that of Bright's disease. The earlier manifestations include headache, epistaxis, increased arterial tension, pale and abundant urine of

low specific gravity, containing a small amount of albumin, slight œdema over the malleoli, etc. Later on there may be dyspnœa, hæmorrhages, broncho-pneumonia, albuminuric retinitis, and vomiting.

The unexpected appearance of mercurial stomatitis in a patient who has been taking mercury for some time should draw attention to the kidneys.

In amyloid disease there is polyuria, with urine of low specific gravity, diminished urea, and an absence of casts.

Diagnosis.—In the absence of definite signs or history of syphilis, the occurrence of symptoms of Bright's disease in a patient who is not gouty, saturnine, or alcoholic is suggestive of syphilis. As Mauriac remarks, 'one does not always find syphilitic antecedents, but it is often necessary to act as if one had found them.'

Uræmic encephalopathy may resemble certain forms of cerebral syphilis. Hence, when brain symptoms occur in a syphilitic it is necessary to think of the kidney as well as the brain. However, syphilitic encephalopathy is usually of slower evolution, and tends to paralysis; uræmic encephalopathy has rather a tendency to dyspnœa and coma. Convulsions may occur in either case, but are more generalized in uræmia.

Tertiary renal syphilis has sometimes been mistaken for malignant disease of the kidney. Margulies mentions a case in which a renal sarcoma was diagnosed in a woman of twenty-six; the supposed sarcoma, however, disappeared under antisyphilitic treatment. Israel also reported two cases in which a kidney tumour was felt and malignant disease diagnosed. Nephrectomy was performed, but both kidneys were found to be affected with tertiary syphilis.

Treatment. — In secondary syphilitic nephritis mercury should be administered with caution at first, owing to the danger of mercurial intoxication from deficient elimination of mercury by the damaged kidneys. The mouth should therefore be carefully watched for signs of stomatitis, which is liable to occur suddenly if there is renal inadequacy. The appearance of stomatitis is an indication for the suspension of mercurial

treatment and the substitution of iodide of potassium in small doses.

Balzer recommends small daily doses of mercury by soluble injections of benzoate or biniodide. Fournier advises inunction combined with iodide internally.

Antisyphilitic treatment should be supplemented as occasion requires by the usual treatment for nephritis (milk diet, rest in bed, purgatives, vapour baths, etc.).

The *amount of urea* should always be measured in cases of syphilitic nephritis, as a fall in urea is an indication for suspending the administration of mercury. A large amount of albumin does not contra-indicate mercurial treatment, so long as the urea remains about normal. In tertiary renal syphilis mixed treatment is indicated.

Prognosis.—Syphilitic nephritis often yields rapidly to specific treatment, but some cases resist it and end fatally. Nephritis must therefore be regarded as one of the most formidable manifestations of the secondary period. The prognosis depends on the state of renal permeability, rather than on the amount of albumin, and a fall in urea and the development of uræmic symptoms are signs of evil omen. Fournier records ten fatal cases out of thirty, all occurring in the first year of syphilis.

The Syphilitic Factor in Bright's Disease.

That syphilis is *one* factor in Bright's disease appears obvious, although this is not sufficiently recognised, and is almost completely ignored in most of the text-books.* The point to be determined is to what extent syphilis is a factor in the causation of what is generally known as Bright's disease, or chronic interstitial nephritis. Rathery, writing in the most recent work on diseases of the kidney, remarks that 'it is often very difficult to estimate the part taken by syphilis in the development of renal lesions. An old syphilitic affected with Bright's

* In the last edition of Green's 'Pathology,' edited by Bosanquet, it is, however, stated that chronic interstitial nephritis is associated 'perhaps more often than is generally believed with syphilis.' Osler also mentions syphilis as a factor in chronic interstitial nephritis.

disease often carries a more or less heavy "etiological baggage" (scarlatina, influenza, typhoid, lead, gout, renal lithiasis, etc.), and it is not easy to unravel what is due to syphilis.'

The chief causes of chronic nephritis given in the text-books are gout, alcohol, lead-poisoning, and exposure to cold. With regard to the last cause (*nephritis à frigore*), Dieulafoy thinks it probable that many such cases are really manifestations of early syphilis. Exposure to cold has been aptly called 'the last refuge of destitute etiology.'

Leonard Guthrie considers it an open question whether gout and lead are actual causes of granular kidney. It may be that the subjects of granular kidney are specially liable to suffer from gout and lead-poisoning, owing to renal inadequacy. Alcohol is possibly the result, rather than the cause, of nephritis; for polyuria is common in interstitial nephritis, and this begets thirst, and thirst leads to alcohol. Guthrie concludes as follows: 'On the whole, although the evidence is far from being conclusive, I am inclined to think that chronic interstitial nephritis in young children is due to hereditary syphilis; and, if so, hereditary or acquired syphilis may also account for many cases of granular kidney in adults.'

Castaigne regards alcohol as a factor of secondary importance in the causation of chronic nephritis; and with regard to gout he remarks that 'to penetrate the pathology of gouty nephritis it is necessary to know to what the attacks of acute gout are due. But on this point we are ill-informed, and it is the whole pathology of gout with which we are concerned.'

Concerning lead-poisoning, even if it does lead to chronic nephritis, the number of patients affected with saturnism is a drop in the ocean compared with those who are syphilitic.

Another point in favour of the syphilitic origin of chronic nephritis is the frequent presence of granular kidney in cases of general paralysis. Beadles, at the Colney Hatch Asylum, found granular kidney in many post-mortems on insane subjects, especially in general paralytics. As general paralysis is now universally recognised as of syphilitic origin, the presence of granular kidney may have been also due to the same disease.

Taking all this evidence into consideration, it would appear not unreasonable to regard syphilis, or heredo-syphilis, as the main factor in the production of chronic nephritis. Further, the frequent presence of endarteritis and periarteritis, which has been found by several observers, would tend to the view that the nephritis is primarily of vascular origin, as is the case with other syphilitic lesions. It may be remembered that the vascular origin of nephritis was urged by Gull and Sutton and Johnson in 1872, and the 'arterio-capillary fibrosis' which they described may have been syphilitic arteritis, although they did not attribute it to this cause.

Gull and Sutton pointed out that the essential features in Bright's disease were more or less general changes in the vascular system throughout the body, and that atrophic changes in the parenchyma of the kidney were secondary. 'In the walls of the minute arteries and also outside and around them there appears to be an excess of fibroid tissue.' Huchard also says, 'Interstitial nephritis, before becoming a disease of the kidneys, is an affection of the cardio-arterial system.' As syphilis is essentially a disease which affects the vascular system, it is rational to regard it as an important factor in the causation of Bright's disease. Hermanides regards chronic interstitial nephritis as parasyphilitic, and due to parasyphilitic endarteritis.

The Suprarenal Capsules.

The suprarenal organs are more often affected in hereditary than in acquired syphilis, but sclerosis and pericapsulitis have been reported in the adult. Brault and Decloux reported a case of perisuprarenal syphiloma forming a caseous mass which extended to the liver and kidney. The capsule was thickened and miliary gummata were present.

Gaucher has reported cases with symptoms of Addison's disease in syphilitics which improved under antisyphilitic treatment. Hence syphilis of the suprarenal organs may be one cause of Addison's disease.

Jacquet has recently found the *Spirochæta pallida* in the suprarenal glands of an adult. The patient had secondary syphilis

with signs of Addison's disease, which yielded to mercurial treatment. Death was due to cerebral hæmorrhage, and the suprarenals were found sclerosed.

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under the skin. Owing to the blood-supply of the bone being cut off from obliteration of the Haversian canals, extensive necrosis may occur, and the sequestrum, when separated, can be diagnosed as syphilitic by its worm-eaten surface. In some cases the implication of the dura mater sets up localized meningitis, which causes one form of syphilitic epilepsy.

Cases of extensive syphilitic caries and necrosis of the skull, many examples of which can be seen in the museums, are not so common nowadays, possibly owing to improvement in therapeutic methods, or possibly owing to the disease having become altered in type. However, a remarkable case was recently shown by Mr. Hutchinson, junior, at the Clinical Society (January 27, 1905). In this case there was extensive necrosis of the skull, causing an intracranial abscess, but no cerebral symptoms: a man contracted syphilis at the age of eighteen, and was only treated for a short time; four years later he suffered from rupia, arthralgia, and iritis: treatment was resumed, and he remained free from symptoms till 1904, when a swelling formed in the vertex, followed by sloughing of a circular patch on the scalp and necrosis of the bone: the cerebral pulsations were visible, but the patient had no cerebral symptoms and continued to work: the bone was removed by trephining, and a large abscess between the skull and dura mater was evacuated.

Traumatism is a common exciting cause of syphilitic periostitis and osteitis, and this explains the occurrence of lesions in the bones of the skull, the tibia, sternum, clavicle, etc. For example, syphilitic periostitis of the clavicle is often seen in porters and others who carry heavy weights on the shoulder. Syphilitic bone lesions are not always recognised during life, especially those of gummata of the dura mater affecting the internal layer of the cranial bones, without periostitis of the cranium. But in most cases, when subcutaneous bones are affected, there is well-marked pain, with nocturnal exacerbations and tenderness on pressure. Compression of a nerve passing through a bony canal will give rise to severe neuralgia.

Small, hard swellings on the anterior surface of the *sternum* are usually syphilitic, although tuberculous osteitis of the

sternum is said to be not uncommon. Suppuration may occur in syphilitic periostitis of the sternum, as in the case of other flat bones, and fragments of bone may be discharged through a fistula.

Perforation of the palate and destruction of the nasal bones from tertiary syphilis affecting these regions is described in Chapter VIII.

The Muscles and Tendons.

Tenosynovitis. — In the course of secondary syphilis inflammation of the tendon sheaths may occur along with periostitis and arthralgia. There may be simple effusion into the tendon sheath, bilateral or unilateral, and generally affecting the extensor tendons of the fingers; or the condition may be acute tenosynovitis, usually affecting the extensor tendons of the fingers or toes, the biceps, or the peronei; less commonly the tendons about the knee-joint or the tendo Achillis.

Myositis. — Fournier describes syphilitic *myosalgia*, or muscular pains, as occurring in secondary syphilis, and characterized by nocturnal exacerbations. *Contracture of the biceps* muscle is also said to occur in secondary syphilis, with flexion of the elbow and great pain on attempts at extension. This condition is said to be of insidious onset, remaining stationary for a long time, and gradually subsiding.

Interstitial myositis and gummata occasionally affect the muscles; but the chief form of muscular syphilis is that affecting the *heart*, in the form of interstitial myocarditis and gummata of the heart muscle (p. 104). Tertiary syphilis of the tongue would also come under this category.

The coincidence of myosalgia, arthralgia, tenosynovitis, and periostitis constitute a syndrome closely resembling ordinary rheumatism, and which Fournier has named *syphilitic pseudo-rheumatism*. When these symptoms occur, together with a certain amount of fever, which is not uncommon, especially in women, the diagnosis may be difficult in the absence of other signs of syphilis. In fact, both syphilis and gonorrhœa are probably responsible for a good many

of the symptoms which commonly pass under the name of 'rheumatism.'

The Joints.

The joints may be affected both in secondary and tertiary syphilis, but joint affections in the secondary stage are less common than periostitis. The earlier arthropathies include *arthralgia*, *hydrarthrosis*, and the later ones *gummatous synovitis* and *osteo-arthritis*

Arthralgia.—This consists in pain in the joint on movement, without any objective changes. It occurs during the first months of the disease, at the same time as the earlier cutaneous eruptions. It is more commonly observed in women, and appears to be independent of previous rheumatism. The principal joints affected are the shoulder, knee, wrist, elbow, and ankle. The pain quickly disappears under antisyphilitic treatment, but persists for months, on and off, in untreated cases.

Hydrarthrosis.—This is much more rare than arthralgia, and is constituted by effusion into the joint without any inflammatory phenomena. At its commencement it may be accompanied by some pain and limitation in movement, but it soon becomes painless, and remains so till its termination. The knee is the joint usually affected, and both knees may be involved simultaneously or successively. The effusion soon yields to specific treatment, but may subside spontaneously. Hydrarthrosis is more common in late heredo-syphilis than in the acquired disease.

Subacute Arthritis *(pseudo-rheumatic syphilitic arthropathy)*. —This form also affects the knees, and is manifested by rapid effusion in the joint, with pain and limitation of movement. The reasons for regarding this joint affection as syphilitic, and not as ordinary rheumatism occurring during syphilis, are—(1) the frequent coexistence with other syphilitic manifestations; (2) the rapid subsidence under specific treatment; (3) the absence of other causes or history of rheumatism. It also differs from common rheumatism in only affecting one or two joints, and exclusively the larger ones such as the knee, and in the absence or transient nature of febrile symptoms.

This form of syphilitic joint disease may be sometimes difficult to diagnose from gonorrhœal arthritis, especially as both have a predilection for the knee-joint. In gonorrhœal arthritis, however, the affection is more acute and painful, and there is usually posterior urethritis present, or at any rate a history of recent gonorrhœa. It is also possible for gonorrhœal arthritis to occur during the course of secondary syphilis, when the patient, as not infrequently happens, contracts both diseases at the same time. In any case, mixed treatment with mercury and iodides is useful in both complaints (*vide* Chapter XXVI.).

Gummatous Arthritis.—This is the most common form of syphilitic arthritis, and generally affects the knee. The subsynovial cellular tissue and periarticular fibrous tissue are infiltrated with gummatous deposits, which can be felt in the form of lumps on each side of the ligamentum patellæ. According to Lancereaux, the synovial membrane itself is not sensibly affected, but the cartilages of the joint are eroded. There is secondary effusion into the joint.

The affection is insidious in onset, and manifested only by slight pain in the joint and limitation of movement. If neglected, ankylosis may occur, owing to changes in the cartilage, which becomes fibrillated and pitted (chondro-arthritis of Virchow). In some cases the gummata may break into the joint and set up acute arthritis. The neighbouring bursæ, in front of and behind the ligamentum patellæ, are liable to become involved in the gummatous infiltration. When the elbow-joint is affected, the olecranon bursa may be involved, and gummatous infiltration of the epitrochlear hollow may cause neuritis of the ulnar nerve.

Osteo-arthritis.—In this form, which is comparatively rare, there is gummatous osteitis of the articular ends of the bones. The knee is the joint most commonly affected, as in the other forms of syphilitic joint disease, and in this case the lower end of the femur is usually the seat of the gummatous process. The gummatous osteitis affects both the epiphysis and the diaphysis, causing enlargement of the bone above the knee-joint. The synovial membrane is not affected, but

effusion of fluid into the joint may take place later. Pain is slight or absent, and limitation of movement, if present, is due to the mechanical obstacle of the enlarged bone. Muscular atrophy is more marked than in the synovial form of arthropathy. The enlargement of the joint is usually preceded by nocturnal pains. In untreated cases the gummata may break into the joint, or may form superficial sinuses.

Diagnosis.—The perisynovial form of gummatous arthritis may resemble *tuberculous disease* of the joint; but the latter differs in causing a general thickening of the synovial membrane, instead of the local gummatous nodules; it is also more rapid in progress, more painful, and causes earlier disablement of the joint. The syphilitic joint usually preserves its mobility, and the patient seldom has to lie up; also, there is no suppuration, unless gummata break into the joint.

Rheumatoid arthritis is more chronic, and causes more bony deformity. The grating of the joint and 'lipping' of the edges of the bone, which are characteristic of rheumatoid arthritis, are absent in syphilitic arthritis.

The osteo-arthritic form may be mistaken for *osteosarcoma.* J. Hutchinson, junior, mentions a case in which amputation was performed for a case of this kind which occurred in a patient with a family history of malignant disease. The growth did not yield to specific treatment, but after amputation gummatous infiltration was found in the bone. The moral of this case is twofold: (1) not to attach too much importance to family history; (2) not to be in a hurry for the effects of 'specific treatment,' which is usually carried out in a rule-of-thumb manner by means of inadequate doses.

Syphilitic joint disease is probably more common than is generally supposed, and requires intensive mixed treatment, by mercurial inunction or injections, combined with large doses of iodide of potassium. Howard Marsh remarks that there is 'good reason to believe that not a few instances of joint disease which resist treatment by the usual methods of blistering, etc., and which show an obstinate tendency to relapse, are examples of syphilis.'

Syphilitic Spondylitis.—This was described by Portal in 1797 under the name of 'syphilitic Pott's disease.' It con-

sists in gummatous osteitis of the vertebræ, causing secondary affection of the spinal cord by extension to the meninges, or by the effects of pressure. It may be due to extension of the syphilitic process from a gummatous ulceration at the back of the pharynx. When localized in the cervical region, it may give rise to paralysis of all four limbs; when in the dorso-lumbar region, to paralysis of the lower limbs only. As in tuberculous Pott's disease, the paralysis soon becomes spastic.

Froelich records two cases of syphilitic cervical spondylitis:

1. A male, aged thirty-five, had a chancre and secondary syphilis in 1892; gummata of the tibia, frontal bone, clavicle, and sternum in 1895. In 1900 symptoms of stiffness of the neck and dysphagia appeared, with an abscess at the back of the pharynx, from which pus was expectorated. Small pieces of bone came away from the pharyngeal fistula. A year later the fistula closed, but the stiffness of the neck persisted.

2. A girl had meningitis at the age of three years. At the age of fifteen she had pain and rigidity of the neck and dysphagia, with œdema of the suboccipital region; under mercury and iodide the symptoms subsided, except the stiffness in the neck.

Diagnosis.—Syphilitic spondylitis differs from tuberculous in not usually causing destruction of the whole body of a vertebra, and in consisting of more disseminated lesions affecting the articular processes and body of the vertebra. There is, therefore, usually an absence of the angular deformity met with in tuberculous caries. In the early stages, however, diagnosis may be difficult, and depends chiefly on the history and other signs of syphilis. In any case, specific treatment should be given a trial.

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CHAPTER XI

THE NERVOUS SYSTEM

The knowledge of syphilis of the central nervous system, although this was noticed by Van Swieten in 1772,* is of comparatively recent date, and it was not until the latter half of the nineteenth century that the subject became fully understood. The chief writers on the subject were Virchow, Broadbent, Buzzard, Wilks, Moxon, Hughlings Jackson, Gowers, Charcot, and Fournier. More recently the subject has been studied by Raymond, Nonne, Babinski, Erb, Nageotte, Widal, and many others on the Continent, and in this country by F. W. Mott, Gowers, Ferrier, etc.

Affections of the nervous system are the most important of all the manifestations of syphilis; first, on account of their frequency and disastrous results; secondly, because of their insidious development, which renders early diagnosis necessary in order to give antisyphilitic treatment a reasonable chance of success. As Fournier remarks, 'Syphilis is a veritable poison to the nervous system.'

Syphilis is the chief factor in organic diseases of the nervous system, and one of the principal causes of insanity. Professor Raymond, of the Salpêtrière Hospital, Paris, remarks as follows: 'Si nous parvenions à supprimer la syphilis et l'alcoolisme du même coup, nous supprimerons le plus grand nombre des maladies nerveuses, en particulier la paralysie générale et le tabes.'

* 'Sæpe observantur cerebri læsiones in lue venerea inveterata, a levissima vertigine, ad lethalem apoplexiam usque, pessimam epilepsiam, cæcitatem, surditatem' (Van Swieten, 'Commentarii,' 1772, vol. v., p. 404).

The syphilitic virus may affect the central nervous system in two ways: first, by causing specific inflammation of the membranes and bloodvessels—syphilitic meningitis and syphilitic arteritis—giving rise to occlusion of the vessels and subsequent degeneration of the nerve elements, and by causing gummata in various parts of the brain and membranes; secondly, by lowering the vital energy of the cells and giving rise to the group of parasyphilitic affections, the most important of which are tabes, general paralysis, certain forms of epilepsy, and possibly other obscure nervous affections of doubtful origin (see Chapter XII.).

In Fournier's statistics of 4,700 cases of tertiary syphilis the nervous system was affected no less than 2,009 times. Cerebro-spinal syphilis is most common in the first six years of the disease, having its maximum frequency in the *third year*. Tabes and general paralysis, on the other hand, appear later, usually between the sixth and twelfth years.

Apart from organic disease of the nervous system, Fournier describes certain *functional disorders* as occurring in secondary syphilis.

The chief of these are—(1) headache; (2) neuralgia, chiefly affecting the supra-orbital, maxillary, and lingual nerves; (3) neuritis, especially of the ulnar nerve, causing neuralgic pains and paresis of the muscles supplied by the ulnar nerve; (4) sciatica; (5) analgesia, especially occurring in women and nervous subjects, and characterized by its symmetrical distribution and partial character; (6) muscular tremors; (7) recrudescence of pre-existing neurosis, especially hysteria.

The Brain.

Cerebral syphilis usually manifests itself between the third and tenth years of the disease, but often occurs in the first year—even as early as the fifth month (see table on p. 242).

Predisposing Causes. — Excessive physiological activity and morbid excitation of the brain are predisposing causes of cerebral syphilis. Alcoholic and venereal excesses, and mental strain from overwork or emotion, may act in this way. Fournier

mentions cases of cerebral syphilis which he attributed to the mental tension caused by the Siege of Paris; also the case of a physician who predicted his own cerebral syphilis from excessive brain-work—a prediction which was justified by the event. The same causes may lead to a recurrent attack of cerebral syphilis; for instance, in a case recorded by Fournier, a man who had been cured of syphilitic hemiplegia by prolonged treatment married and 'made up for lost time,' with the result that a second attack of hemiplegia occurred and proved fatal. But the chief secondary factor in cerebral syphilis is *alcoholism*. As Fournier observes, 'alcohol is the born enemy of syphilis.' Injuries to the head may also act as exciting causes.

It was pointed out by Broadbent that cerebral syphilis usually occurs in cases in which the secondary period is mild. This is probably explained by the fact that patients with mild secondary symptoms usually neglect treatment; and it is has been shown by Fournier that *the chief cause of tertiarism is insufficient treatment*.

This is shown by the following statistics: Out of 2,396 cases of tertiary syphilis observed by Fournier, 1,878 had undergone either no treatment at all, or had been treated for periods of less than a year's duration; while 63 cases only had been treated for upwards of three years. In other words, only 3 per cent. of the cases had received adequate treatment (see Chapter XIV.).

These figures seem to show conclusively that the chief factor in the development of tertiary symptoms is insufficient treatment, and they emphasize the necessity for more prolonged treatment than is usually undergone.

Pathology.—The specific inflammatory process may begin in the membranes or in the walls of the vessels. According to Nageotte, the meninges are primarily affected, and this is shown by the presence of lymphocytosis in the cerebro-spinal fluid. Syphilitic meningitis is always accompanied by changes in the vessels, but arteritis may occur without meningitis.

Meningitis.—Syphilitic meningitis affects the base of the brain much more commonly than the convexity, and occurs

especially in the interpeduncular space and in the Sylvian fissures. It may extend down the membranes of the spinal cord. Mott points out that the parts affected are where the cerebro-spinal fluid is most abundant. 'Inflammatory exudation about the base of the brain would tend to close the foramina of Magendie and interfere with the escape of fluid from the ventricles, thereby causing internal hydrocephalus. This condition may account for the stupor, drowsiness, paresis, and dementia, with intervals of comparative sanity; which alternate states may be coincident in the one case with accumulation, in the other with absorption or escape of the fluid.'

Gummata.—The gummatous process nearly always originates in the meninges, and when gummata occur in the substance of the brain, this is explained by their developing in the meningeal extensions which follow the bloodvessels. Gummatous meningitis of the base surrounds the vessels forming the circle of Willis and the cranial nerves with a gelatinous mass, grayish-red in colour. The vessels are affected with endarteritis and periarteritis, and miliary gummata may be seen in considerable numbers.

Larger gummata may occur in any part of the brain, but are more commonly situated at the base near the optic chiasma. They are grayish-red at their periphery and yellow in the centre, owing to caseation. A circumscribed gumma may develop in the dura mater as the result of a blow on the head. In this case there is much thickening of the dura mater, and adhesion both to the skull and to the brain. In this form of cerebral syphilis the symptoms are those of a local lesion, and are more amenable to treatment than more generalized forms.

Syphilitic Arteritis is the chief factor in the pathology of cerebral syphilis. It is most often found in the vessels forming the circle of Willis, and especially in the middle cerebral artery.

Syphilitic endarteritis, by narrowing the lumen of the vessels, causes diminished blood-supply or ischæmia of the parts of the brain supplied by the vessels. Complete occlusion caused by endarteritis, or more often by *thrombosis*, causes necrobiosis, or softening of the corresponding part of the brain.

Cerebral aneurism and cerebral hæmorrhage may also result from syphilitic arteritis, the former by replacement of the muscular and elastic tissue of the vessel by yielding fibrous tissue, the latter from rupture of a vessel extensively affected by arteritis or atheroma.

An important point in cerebral arteritis is that it chiefly affects the origin of *terminal arteries*. Thus, the middle cerebral artery gives off the lenticulo-striate and lenticulo-optic arteries which supply the central nuclei; the posterior cerebral supplies the nucleus of the third nerve, the optic thalamus, optic tract, and corpora quadrigemina; and from the vertebral and basilar arise perforating arteries supplying the nuclei in the fourth ventricle. Endarteritis without obliteration is sufficient to cause, in one of these central vessels, a focus of softening, with fatal consequences. In this way limited foci of softening may be found without arteritis of the vessel itself, but depending on constriction at its point of origin.

Periarteritis causes extension of inflammation to the surrounding tissues, and the extensive cell infiltration may give rise to gummatous meningitis. 'When the membranes are affected by the inflammatory process the vessels are generally also affected, so that we may have a combination of the effects of cerebral softening and vascular occlusion with cortical irritation or cranial nerve paralysis from gummatous meningitis' (Mott).

Symptomatology.—Cerebral syphilis is characterized by the great multiplicity of its phenomena. The symptoms naturally vary according to the seat of the lesion; thus, a basal lesion causes paralysis by implication of the nerves at the base of the brain; a lesion of the convexity of the brain causes epilepsy and mental disorders, and partial cortical paralysis.

The multiplicity of the lesions is shown by a case of Buzzard's, in which there was almost complete paralysis of all the four limbs; double facial paralysis; anæsthesia of the trunk, limbs, and face; incomplete paralysis of respiration and deglutition; difficulty in articulation; and paresis of the bladder. In spite of this multitude of disorders the patient is reported to have been cured.

Cerebral syphilis may commence with headache, vertigo, epileptic attacks, ocular paralysis, hemiplegia, or mental disorders; but the modes of onset may be reduced to six clinical types (Fournier)—(1) the cephalalgic type; (2) the congestive type; (3) the epileptic type; (4) the aphasic type; (5) the mental type; (6) the paralytic type. These types are very often associated together to form mixed types, and in some cases there is an absence of any one predominant symptom.

Later on the phenomena become more complex, and at the same time more uniform, by the fusion of the initial types. Finally, cerebral syphilis, if left to its own evolution, tends to cerebral softening and paralytic dementia.

Although possessing no absolute pathognomonic sign, cerebral syphilis is characterized by the following points:

1. Premonitory headache, with nocturnal exacerbations.
2. Epileptic attacks occurring at adult or middle age, and characterized by their partial nature and by the absence of loss of consciousness.
3. Paralysis of the ocular muscles.
4. Optic neuritis.
5. Partial and multiple paralysis of irregular distribution.
6. Aphasia.
7. Mental disorders, including sudden or progressive loss of memory.
8. Early hemiplegia, usually occurring without loss of consciousness, and often incomplete.
9. Rapid changes in the general health and physiognomy, loss of flesh, anæmia, etc.
10. The frequent coexistence of different cerebral symptoms —*e.g.*, (*a*) hemiplegia, with ocular paralysis; (*b*) double hemiplegia; (*c*) epilepsy, with ocular paralysis; (*d*) mania, with strabismus; (*e*) mental disorders, with hemiplegia or ocular paralysis.
11. The beneficial results of antisyphilitic treatment.
12. The slow and progressive evolution.
13. The frequency of relapses and recurrences.

Cerebral syphilis may terminate in—(1) complete cure;

(2) incomplete cure; (3) permanent disablement, mental or physical; (4) blindness on both sides; (5) deafness on one side; (6) death. In 90 cases of cerebral syphilis observed by Fournier the results were 14 deaths, 30 cures, and 46 incomplete cures, or permanent disablements. Cases of incomplete cure with 'relics' may occur both in treated and in untreated cases. They include diminution in intelligence and memory, weakness on one side of the body, facial asymmetry, impediment in speech, strabismus or mydriasis, diminution in visual acuity, and partial deafness.

An instructive case of disastrous 'relics' is mentioned by Fournier: A young student contracted syphilis, and was insufficiently treated. A few years later cerebral syphilis developed, with headache, delirium, optic neuritis, and hemiplegia. Under treatment all the signs disappeared, except the optic neuritis; this persisted, and the patient was left permanently blind at the age of twenty-five.

In the absence of treatment there is a progressive evolution towards disorganization. The initial forms may become permanent, and constitute permanent cranial paralysis, hemiplegia, epilepsy, or insanity, without the supervention of other symptoms. There is a tendency, however, for the initial forms to combine and form complex syndromes; for instance, the epileptic form may end in psychic or motor disorders, the mental form may end in paralysis, and inversely the paralytic form may be complicated by mental disorders.

The Cephalalgic Type.—In this type headache is the predominant symptom. The *syphilitic headache* is of the greatest importance, as its early recognition and treatment may arrest the progress of cerebral syphilis, and save the patient from paralysis or mental breakdown. This form of headache is characterized (1) by its *intensity;* (2) by its *persistency;* (3) by its *nocturnal exacerbations.*

The pain is sometimes likened to a weight on the head; sometimes to compression of the head in a vice; at other times to blows on the head with a hammer. It may be circumscribed, 'like a nail driven into the head,' or diffuse. Sometimes it is accompanied by quiet or noisy delirium. The

nocturnal exacerbations are a characteristic feature, but are not constant, so that their absence does not exclude syphilis as the cause of the headache. The intensity and long duration is of more importance in diagnosis, the attacks sometimes occurring for several years before the supervention of further cerebral mischief.

Syphilis may cause headache in several ways—(1) by periostitis of the cranial bones ; (2) by implication of a nerve in a bony canal ; (3) by meningitis ; (4) by syphilitic arteritis. The last two lesions are those which give rise to the characteristic headache of early cerebral syphilis, which is distinguished from the other forms of headache by being diffuse, intense, persistent, and worse at night.

The headache of *periostitis* is localized to certain points ; the headache of *neuralgia* is characterized by painful points along the course of certain nerves ; the headache of *hysteria* is variable, and generally curable by contrary suggestion ; the headache of *neurasthenia* (which may itself be parasyphilitic) is matutinal, and accompanied by subjective sensations. Headache may also be due to urinary insufficiency from syphilitic nephritis, but this uræmic headache has not the characters of the true syphilitic headache.

The Congestive Type.—This is characterized by the following symptoms :

1. Motor affections, such as stumbling when walking, difficulty in descending stairs, loss of equilibrium, stuttering speech, weakness in the muscles and fatigue, want of precision in movements, sometimes staggering gait suggesting alcoholic intoxication, and sometimes paresis of the intestines and bladder (the latter may be mistaken for stricture).

2. Sense affections, such as vertigo, dizziness, buzzing in the ears, resembing Ménière's disease ; sometimes nausea and vomiting ; muscæ volitantes, etc.

3. Disorders of sensation, including numbness and tingling, especially in the fingers ; vague pains in the limbs simulating rheumatism.

4. A condition ot cerebral uncertainty with transient eclipse of intelligence, resembling *petit mal*, but differing in the

absence of pallor and fixed regard of the latter; mental obnubilation and loss of memory.

These attacks, at first transient, may become more frequent, and even permanent if untreated. The congestive form of cerebral syphilis is often the prologue to later phenomena, such as epilepsy, aphasia, and paralysis; but it may continue in the same form for a considerable time.

As a rule, it is followed by partial paralysis; for instance, paralysis of the third nerve, causing ptosis, mydriasis and strabismus, facial hemiplegia (paralysis of the tongue with scanning speech), monoplegia (affecting one hand or single fingers only), and partial hemiplegia. These attacks may last only a few hours, and consist more in paresis than paralysis. Congestive 'strokes' may also follow, consisting in sudden loss of muscular power, and falling, with or without loss of consciousness. A congestive or apoplectic stroke with loss of consciousness is generally followed by permanent paralysis.

Sudden *coma* may be one of the first signs of the congestive form of cerebral syphilis, without any premonitory symptoms. This is rare, but is important to bear in mind, as it may be amenable to treatment with large doses of iodide.

The Epileptic Type.—An epileptic attack may be the first sign of cerebral syphilis. Epilepsy appearing for the first time after the age of thirty is practically always due to syphilis, the so-called 'essential epilepsy' always appearing before adult age. The epileptic form of cerebral syphilis may remain for a time without complication by other phenomena, and Fournier records a case in which it remained so for four years. More often, however, it is followed by other cerebral symptoms —congestive, mental, or paralytic.

There are usually premonitory symptoms of headache, somnolence, and changes in the general health. The most usual prodromal symptom is the *syphilitic headache*, which may precede the epileptic attacks by several weeks or months. Sometimes this headache is limited to the temporo-parietal regions, and may be mistaken for migraine or neuralgia.

The fits occur at first at long intervals, but later on become more frequent. They are generally preceded by an aura,

which may take the form of tingling sensations, noises in the ears, flashes of light, muscular tremors, and abnormal sensations in the limbs.

Syphilitic epilepsy is often unilateral, and not accompanied by loss of consciousness. In this case the attacks are always on the same side, and signify a localized lesion in the motor area. This explains the frequent occurrence of the prodromal pain in the temporo-parietal region. The upper limb is affected more often than the lower limb or face. Owing to the retention of consciousness, pain may be severe.

Such attacks are generally the prelude to more complete crises with loss of consciousness; also there may be alternate attacks of partial and complete epilepsy. Brouardel mentions the case of a man of forty who had a chancre and secondary syphilis in 1871. In 1874 he was attacked with convulsions of the right arm, lasting a few minutes, and not accompanied by loss of consciousness; a second attack occurred in fifteen minutes, and a third after the same interval, but the latter was accompanied by loss of consciousness. During the next few days he had two epileptic attacks, unilateral and without loss of consciousness. In 1875 he had two similar attacks, less intense than the former. This case illustrates the fact that consciousness may be alternately retained and lost during attacks of syphilitic partial epilepsy.

An epileptic attack is sometimes followed by permanent loss of memory, and in a case mentioned by Fournier, a patient, after an attack of syphilitic epilepsy, forgot all the incidents of the Siege of Paris. Other sequelæ are progressive hebetude, maniacal excitement, temporary paresis of the muscles of the face or limbs, and, later on, definite paralysis of the muscles of the eye, or hemiplegia. The usual termination is hemiplegia.

Some attacks of syphilitic epilepsy resemble those of 'essential epilepsy,' with the typical signs of *grand mal* (loss of consciousness, tonic convulsions of short duration, followed by clonic convulsions of longer duration, frothing at the mouth, biting the tongue, stertor, rapid return to consciousness, and slight after-symptoms of impaired memory). At other times attacks of *petit mal* may occur (sudden attacks of vertigo,

mental eclipse, faintness, trembling or spasms of muscles, and occasionally attacks of fury). These attacks of *petit mal* may occur alone in the early periods of the disease, or later on may alternate with attacks of *grand mal*.

Diagnosis.—The chief differences between syphilitic epilepsy and 'essential epilepsy' are—(1) absence of the initial cry; (2) the later onset in adult life; (3) the early addition of other cerebral symptoms occurring in the intervals between the attacks; (4) the frequent unilateral character, without loss of consciousness; (5) the effect of antisyphilitic treatment. Syphilis is the only cause to explain the sudden onset of epilepsy in a healthy adult; hence the rule should be to treat all such cases for syphilis, even in the absence of any history.

Hughlings Jackson does not regard loss of consciousness as an important distinction in cases of epilepsy. He remarks: 'I would here urge again that the absolute distinction of epilepsies into cases in which consciousness is lost and cases in which it is not lost is not a distinction of either anatomical or physiological parentage. It is probably due to the common metaphysical habit of mind which considers consciousness to be an entity.' It therefore appears that the main difference between syphilitic and 'essential epilepsy' becomes reduced to the presence or absence of other signs of cerebral syphilis. Moreover, the so-called 'essential epilepsy' may be due to *parasyphilis*. This question is discussed more fully in the next chapter.

The Aphasic Type. — Aphasia may occasionally be an isolated symptom at the onset of cerebral syphilis, but is more often associated with other symptoms, such as headache, vertigo, and especially right hemiplegia. In some cases there are repeated attacks of transitory aphasia, accompanied by paresis of the right side. Buzzard reports a case in which six attacks of aphasia occurred during two months, all accompanied by right-sided paresis.

Aphasia occasionally occurs with left hemiplegia, monoplegia, ocular paralysis, or paraplegia. Such cases are rare, and due to multiple lesions. Aphasia may also be associated with epilepsy, with or without right-sided paralysis.

Fournier mentions the case of a young man (syphilitic for eight years and incompletely treated) in whom cerebral syphilis commenced with aphasia, which was followed in a few weeks by epilepsy and right hemiplegia. Further attacks of aphasia occurred, with loss of memory and intelligence. This case was cured by antisyphilitic treatment.

Sometimes aphasia is associated with paralysis of the tongue (glossoplegia). For instance, in a case of Fournier's multiple attacks of aphasia occurred, with incomplete glossoplegia and paresis of the orbicularis palpebrarum. The aphasic attacks lasted from fifteen to thirty minutes, but the lingual and palpebral paralyses were permanent. The faculty of speech was preserved, but speech was embarrassed. In such cases there is simultaneous affection of the centre for speech and the motor centre for the tongue in the third frontal convolution.

The Mental Type.—'In the great majority of cases in which syphilis attacks the brain it affects the mind in various degrees and in various forms. It often affects it from the beginning, or soon after the first attack. If it respects it for a certain time, it seldom fails to affect it at a later period, when the disease is abandoned to itself, or when it continues its progressive evolution in spite of treatment' (Fournier).

The mental symptoms may remain isolated for a time, but are generally associated with other phenomena. There are two chief forms—(1) slow evolution, with progressive mental failing; (2) more rapid evolution, with signs of exaltation, delirium, or mania. The former is the more common, and is characterized by loss of memory and want of connection in ideas, speech, and action; in fact, a condition of mental asthenia or cerebral obnubilation, of which the patients are conscious in a vague manner. There is also a change in the character and moral disposition.

Amnesia is common, and may occur at various periods in cerebral syphilis. It may be gradually progressive, or may occur in irregular attacks, especially in epileptic or apoplectiform seizures. It varies in degree from partial to complete loss of memory.

Incoherent hebetude, or mental depression with incoherence

affecting all the acts of life, is seen especially in association with the epileptic and paralytic forms of cerebral syphilis. In some cases there may be melancholia or a suicidal tendency.

Delirium.—In some cases the psychic symptoms of cerebral syphilis are limited to delirium analogous to that occurring in febrile diseases, such as meningitis or typhoid; hence the possibility of mistaking delirium due to cerebral syphilis for febrile complaints, for this delirium may for a time be the only sign of cerebral syphilis.

A case in point is one for which I am indebted to Dr. J. D. Rolleston. A patient in a state of violent delirium was sent to one of the London fever hospitals as a case of enteric fever. He had been delirious for about three weeks, after an attack of severe headache. On admission, the remains of a chancre on the penis was found, together with a secondary eruption and left ptosis. The temperature was normal.

In other cases there is cerebral excitement without delirium, which causes the patient to act in an eccentric manner in various ways. This may reach the degree of *maniacal excitement*, characterized by extravagance in words and acts, and may end in all the symptoms of acute mania. These cases are sometimes fatal in a few weeks.

The Paralytic Type.—'The paralytic form is a common type, towards which all other forms of cerebral syphilis converge at a certain period of their natural evolution' (Fournier).

Paralytic phenomena are sometimes primary, but more often secondary, and affect three chief forms—(1) paralysis of the cranial nerves; (2) monoplegia; (3) hemiplegia.

The Cranial Nerves.—Syphilis has a predilection for the nerves of the eye, especially the *third nerve*. Paralysis of the ocular nerves is often an early sign of cerebral syphilis; it is insidious in onset and rapid in development, often partial or incomplete. Mydriasis may be the only sign; but there is often coexistence of several ocular paralyses in the same subject.

The Optic Nerve.—Affection of the optic nerve may vary from slight amblyopia to complete blindness. Visual troubles

may form the first sign of cerebral syphilis, but are more often associated with other cerebral phenomena.

Optic neuritis is a common sign of cerebral syphilis, and signifies a cerebral lesion behind the optic nerve. Vision may remain intact even with double optic neuritis; hence the importance of ophthalmoscopic examination in all cases of syphilis.

A characteristic type of cerebral syphilis consists in the coexistence of paralysis, headache, epileptic attacks, and vomiting.

The Auditory Nerve.—In the early stage of cerebral syphilis affection of the auditory nerve may be manifested by buzzing or whistling noises in the ears, on one or both sides. Later on there may be diminution of hearing up to complete deafness, but the latter is always unilateral.

The Facial Nerve.—This is sometimes affected, causing facial hemiplegia.

The Hypoglossal Nerve.—Ephemeral lingual paresis due to affection of the hypoglossal nerve is common in the early stages of cerebral syphilis. Glossoplegia is also often associated with hemiplegia.

The Vagus Nerve.—This may be affected by cerebral syphilis. Fournier mentions a case with repeated and obstinate vomiting, dyspnœa, and slow pulse, which he attributed to affection of the vagus nerve. Broadbent has also recorded a case of persistent hiccough occurring in cerebral syphilis, and probably due to affection of the vagus. Paralysis of the vocal cords may also occur (p. 157).

Monoplegia is common in the early stages of cerebral syphilis in the form of transitory paresis. More rarely it remains as a permanent paralysis after a transitory attack of hemiplegia.

Hemiplegia.—This is one of the most common results of cerebral syphilis, and is usually due to endarteritis and thrombosis of the middle cerebral artery, more rarely to pressure by gummata. Its period of maximum frequency is between the sixth and tenth years of the disease, but cases have been reported as early as the sixth month.

Hemiplegia may be transient or permanent: it may be the

initial symptom or the final one; sometimes it predominates over other symptoms, at other times it is subordinate to them.

The onset of hemiplegia is usually preceded by prodromal symptoms, which may consist in headache, tingling, numbness, and sensation of cold in the limbs; transient paresis of the eye muscles, tongue, facial muscles, and limbs. The invasion of hemiplegia is sudden, and usually occurs without loss of consciousness. It is progressive, and affects one part of the face and limbs after another successively. It is generally incomplete, and often partial. Sensation is usually intact, but sometimes diminished. Occasionally there is hemianæsthesia of the same side, signifying a lesion in the posterior third of the internal capsule. It may or may not be associated with mental disorders of various kinds and degrees, and hemiplegia often marks the beginning of progressive mental decay. Ocular paralysis (ptosis, mydriasis, and external strabismus) may occur simultaneously, but more often shortly after the hemiplegia. Aphasia is common in right hemiplegia, and amnesia may occur at the same time.

Bilateral Hemiplegia.—This is always due to two successive attacks separated by intervals of weeks or months, and generally affecting the two sides unequally. Hughlings Jackson reported a case of double hemiplegia with an interval of three months between the two attacks. At the post-mortem both the Sylvian arteries were found occluded, with softening of the corpora striata. Other varieties of syphilitic hemiplegia are—*crossed hemiplegia*, affecting the face on one side and the limbs on the opposite side; *intermittent hemiplegia*, in which a series of hemiplegic attacks follow each other at intervals varying from a few minutes to several hours, and then disappear without leaving any trace (Fournier); *hemiplegia with medullary lesions*, in which the hemiplegia is associated with ataxic symptoms.

Diagnosis.—The main characteristic features of syphilitic hemiplegia are—the prodromal headache, transient paralyses, and epileptic attacks; the absence of loss of consciousness; the frequently slow, progressive, and incomplete nature of the paralysis; and the association with ocular paralysis and optic

neuritis. Most cases of hemiplegia occurring between twenty and forty-five are syphilitic (Buzzard); but there is no reason why any age limit should be attached to syphilitic hemiplegia, since syphilis is a disease of all ages; also, according to Fournier and others, tertiary symptoms may occur as late as sixty years after infection. The part taken by syphilis in the causation of atheroma and Bright's disease is discussed in Chapters VI. and IX., and it is probable that the majority of cases of cerebral hæmorrhage are due to degeneration of the vessels largely caused by antecedent syphilis. Therefore, apart from injury, tumours, and valvular disease of the heart, it would appear rational to regard the great majority of cases of hemiplegia as of syphilitic origin.

Syphilitic Insanity.

It would appear obvious that syphilis, owing to its destructive effects on the brain, must be one of the chief causes of insanity; but it is only comparatively recently that this result of syphilis has been recognised, and this chiefly by the establishment of syphilis as the fundamental cause of general paralysis (Chapter XII.). However, apart from general paralysis, it has been stated that syphilis may cause 'all the common forms of insanity, from the most violent mania to the most complete idiocy'; and, as Mott remarks, 'of all the causes of insanity, none writes with such a broad and indelible hand as syphilis.'

The mental type of cerebral syphilis is often incurable, and has a tendency to relative or absolute mental decay, ending in paralytic dementia. Buzzard observes: 'I am persuaded that there exist a great number of subjects who, at the middle period of life, become chronic mental invalids owing to syphilis of the brain.'

Grainger Stewart in 1870 drew attention to syphilitic insanity, and reported three cases, all of which were characterized by the same points—viz., delusions of conspiracy, cruelty, and persecution; hallucinations of touch, hearing, and sight; suicidal tendency, nocturnal exacerbations, and headache. Specific treatment had little effect on these cases.

Before this (1852) cases of mental hebetude, incoherency, and suicidal mania following syphilitic meningitis had been reported by Read of Dublin; and Duncan in 1863 reported cases of mania following epilepsy.

Hughlings Jackson in 1875 described two kinds of syphilitic insanity—(1) negative, consisting in mental conditions, such as imbecility, due to destruction of the brain by syphilitic lesions; (2) positive, consisting in illusions, delusions, hallucinations, and raving. He also remarked that mania may follow paroxysms of syphilitic epilepsy in which there is loss of consciousnesss at the onset of the paroxysm or soon after.

It is also probable that hereditary syphilis plays an important part in the production of insanity, either by causing actual cerebral lesions, or by its dystrophic effects on the brain acting as a predisposing cause to secondary factors (overwork, excesses, etc.) which would not affect a healthy brain. We often read of vague references to 'a hereditary predisposition to nervous disease,' 'a hereditary tendency to insanity,' etc. It would be far more rational to regard these 'hereditary tendencies' as nothing more nor less than a predisposition to nervous and mental disease due to hereditary syphilis. Syphilis is *par excellence* the hereditary disease, 'even unto the third generation,' and is quite sufficient to explain the prevalence of insanity. Considering the predilection of syphilis for the nervous system, it is remarkable that insanity is not more widespread than it is.

Incidents of Localization.

As no part of the brain is exempt from syphilitic lesions, the localization of these lesions to certain areas may give rise to other phenomena which have not been included in the preceding types. These include hemichorea and athetosis, labio-glosso-laryngeal paralysis, polydipsia and polyuria, diabetes, laryngeal paralyses, Ménière's disease, circulatory troubles (weak pulse and coldness of the extremities, etc.).

Hemichorea.—This is always unilateral, and may occur by itself or as a sequel to hemiplegia. Sometimes there is post-

hemiplegic *athetosis*, manifested by involuntary movements in the fingers and toes of the paralyzed limbs.

MÉNIÈRE'S DISEASE.—Hughlings Jackson pointed out in 1875 that 'syphilitic ear disease may cause attacks of vertigo, with reeling and vomiting (Ménière's disease).' This syndrome may be due to a syphilitic lesion of central origin, or one affecting the internal ear.

Balzer has reported a case occurring in a man about nine months after primary and secondary syphilis. The patient was attacked with vertigo, nausea, and vomiting, which continued while in bed, but was not accompanied by loss of consciousness. The vertigo disappeared after eight intravenous injections of cyanide of mercury, but the accompanying deafness and tinnitus persisted.

LABIO-GLOSSO-LARYNGEAL PARALYSIS.—This may occur as a primary affection, or may be secondary to other symptoms. Fournier mentions a case which occurred after right hemiplegia with aphasia. The patient presented the characteristic signs of labio-glosso-laryngeal paralysis—viz., the mouth half open, with the upper lip raised and the lower drooping; running of saliva from the mouth; complete immobility of the tongue; difficulty in mastication and in swallowing; paralysis of the soft palate, with nasal reflux; frequent luxation of the jaw, owing to predominance of the lower muscles. This case was much improved after three months' antisyphilitic treatment, but was lost sight of afterwards. Cheadle also had a similar case in 1870, which resulted in a complete cure.

DIABETES.—Perroud in 1869 reported the case of a woman aged forty-three who suffered from intense thirst and polyuria. The urine, however, contained no sugar. Later on she was affected with headache, vertigo, and visual troubles, and died of hemiplegia and coma six months later. At the autopsy syphilitic lesions were found in the meninges and liver, and five cerebral gummata, one of which was situated in the floor of the fourth ventricle.

The connection between diabetes and syphilis has recently been investigated by Troller, who formulates the following conclusions: (1) Diabetes should not be considered as a

morbid entity, but as a syndrome of varied origin. Syphilis may be considered as a frequent cause of this syndrome. (2) Saccharine syphilitic diabetes may appear in secondary syphilis, but is more common in the tertiary period. (3) In the secondary period there is sometimes transient glycosuria, which in some cases may become true diabetes. Glycosuria is due to disordered metabolism, while diabetes is caused by a cerebral lesion. (4) In tertiary syphilis there are three forms: (*a*) Nervous diabetes, occurring in subjects from twenty to forty years of age, during the first four years of the disease, and accompanied by cerebral phenomena. (*b*) Pancreatic diabetes, occurring fifteen to twenty years after infection. This is of grave prognosis, and is characterized by fibrous pancreatitis with secondary affection of the islands of Langerhans. (*c*) Diabetes without cerebral or pancreatic symptoms, occurring in middle-aged persons fifteen or twenty years after infection. This is of doubtful pathogeny, but it is more amenable to treatment than the other forms. (5) Parasyphilitic diabetes may occur, and is little influenced by specific treatment. (6) In heredo-syphilis diabetes may occur, and is cured by mercurial treatment. Considering the frequency of syphilitic pancreatitis in the subjects of heredosyphilis, this may be the cause. (7) Syphilis may possibly explain the occurrence of conjugal diabetes.

Bosanquet found evidence of syphilis in ten cases out of eighty post-mortems on diabetic patients (*Lancet*, April 8, 1905).

The Spinal Cord.

More than half the cases of disease of the spinal cord are due to syphilis, apart from tabes, which considerably increases the proportion (Gilles de la Tourette).

The clinical forms of spinal syphilis are numerous, and depend more on the localization than on the nature of the morbid processes. The lesions, which are characterized by their irregular distribution, appear to be formed by the association of myelitis with ischæmic degeneration, in which the part played by arteritis is difficult to distinguish (Darier).

Gilles de la Tourette remarks that the secondary degenerations which are produced by syphilis in the different columns follow the ordinary laws of the general pathology of the spinal cord, but in spinal syphilis proper the lesions are not limited to the system of the posterior columns, as in locomotor ataxy; to the pyramidal system, as in amyotrophic lateral sclerosis; to the anterior cornua, as in acute or chronic poliomyelitis. Syphilis attacks the spinal cord in a much more irregular manner. It may invade all the systems at the same time, including the meninges, at different levels; so that even in the best established clinical groups which result from its action, if cases belonging to these groups have a certain family resemblance by which they may be recognised and differentiated, it is no less true that two cases of the same kind are rarely superposable or exactly similar to each other in symptomatic expression.

These facts apply to active syphilis of the spinal cord, but whether amyotrophic lateral sclerosis, multiple sclerosis, poliomyelitis, and other spinal diseases of obscure etiology, are connected with syphilis is another question. Tabes is known to be of syphilitic or parasyphilitic origin, and is probably not peculiar in this respect. This question is discussed in the next chapter.

Syphilis of the nervous system may be limited to the spinal cord, but the brain and cranial nerves are frequently affected at the same time.

The syphilitic process may affect the membranes or the interstitial tissue of the cord itself, constituting syphilitic meningitis and myelitis respectively. The two processes are, however, usually associated together as *meningomyelitis*. The process of cell infiltration may be found to extend along the whole length of the cord, although the lesions appear localized to the naked eye. The dura mater, pia mater, and arachnoid are usually affected at the same time, and more often on the posterior surface of the cord. Both meningitis and myelitis may be diffuse or circumscribed, but the diffuse form is more common than localized gummata. The roots of the spinal nerves may be affected by extension of the inflam-

mation from the meninges, or more rarely by interstitial gummata.

Owing to the irregular distribution of the lesions, the symptoms of spinal syphilis vary considerably. The chief symptoms are pain along the spine and in the limbs, girdle pains, and motor, sensory, and trophic symptoms, depending on implication of the roots of the nerves, and resulting in paresis, contraction and stiffness of the muscles, alteration in the temperature sense, and muscular atrophy. As the disease extends, paraplegia with affection of the bladder and rectum supervene. When the cervical region is affected, there may be quadriplegia, and monoplegia is observed in some cases. The spinal symptoms may be associated with cerebral phenomena, consisting in nocturnal headaches, hemianopsia, diplopia, and affection of the pupils.

Meningomyelitis is not, as was formerly supposed, a late phenomenon of syphilis, but may occur at a comparatively early period. In seventy-four cases collected by Savard the affection appeared twenty-six times from six to eight months after the chancre, nine times between the first and second year, and thirty-nine times after the second year. In other words, nearly half the cases occurred before the end of the second year.

The following are the chief clinical types of active syphilis of the spinal cord:

Hypertrophic Cervical Pachymeningitis.—This is characterized by pains in the neck radiating to the upper limbs, atrophic paralysis of the muscles supplied by the cervical nerves, and paralysis of the hypoglossal nerve with hemiatrophy of the tongue. It may be associated with basal meningitis. This group of symptoms may also be produced by gummatous osteitis of the vertebræ.

Early Malignant Syphilis of the Nervous System.—This term is applied by Gilles de la Tourette to a clinical form affecting the whole of the nervous system at an early period of the disease. It is best illustrated by the following examples:

A man aged forty contracted a chancre of the tonsil in 1890. In November of the same year he presented right

facial paralysis. In February, 1891, in spite of antisyphilitic treatment, he suffered from severe nocturnal headaches. Two months later he had right hemiplegia, which was improved by energetic treatment. Four months after this he was attacked by severe lumbar pain, accompanied by difficulty in walking, formication, increased knee-jerks, and alternate retention and incontinence of urine; in other words, syphilitic paraplegia. In this case all the phenomena appeared in the first year of the disease.

In another case observed by Charcot and Fournier the medulla was also affected:

A woman aged twenty contracted syphilis in January, 1890. In June she had severe nocturnal headaches. In May, 1891, ptosis of the left side and diplopia developed, which disappeared under specific treatment. In September severe pains occurred along the spine, especially in the lumbar region. This was soon followed by paralysis of the upper and lower limbs of the same side, constituting the rare form of *spinal hemiplegia*. A fortnight later ptosis, myosis, and diplopia reappeared. That the paralysis was partly of medullary origin was shown by the presence of obstinate constipation, accompanied by frequent desire to micturate and slight incontinence of urine. The paralysis recovered under specific treatment, but about the same time paralysis occurred in the opposite lower limb (right), with anæsthesia on the left side of the abdomen. This forms the type known as *Brown-Séquard's paralysis*, or *spinal hemiparaplegia with crossed anæsthesia*. Brown-Séquard's paralysis is an uncommon type, but almost always due to syphilis; sometimes to a gumma of one half of the transverse section of the cord. In typical cases, in which one half of the cord is affected, there is motor paralysis on one side and sensory paralysis for pain and temperature on the other side. The bladder and rectum are usually affected. Symptoms of irritation often precede the paralysis, causing hyperæsthesia on the side which afterwards becomes anæsthetic, and rigidity on the side which subsequently becomes paralyzed.

Another example of diffuse syphilis of the nervous system is the case of Charcot and Gombault, in which there occurred

right facial paralysis and paralysis of the left external rectus of the eye, associated with incomplete paralysis of the left lower limb and corresponding anæsthesia of the opposite side (Brown-Séquard's paralysis). There were also present optic neuritis and paralysis of the right sixth nerve and trigeminal neuralgia. At the autopsy there was found partial degeneration of the optic nerves and optic tracts; small gummata in both cerebral peduncles and at the point of emergence of the right motor oculi nerve, which was degenerated. There were also two gummata in the medulla, one in the floor of the fourth ventricle, and another on the lateral fasciculus of the left isthmus. The brain, the bony walls of the vertebral canal, and the dura mater were intact, but there was a patch of leptomeningitis involving the roots of the third dorsal nerve on the left side. At this point there was sclerosis of the medullary parenchyma affecting the lateral column, the gray matter, and the posterior columns. Microscopic examination showed small-celled infiltration, with granular and fatty degeneration of the nerve elements and changes in the walls of the vessels.

This clinical form of syphilis of the nerve centres, the symptomatic expressions of which are so varied, may take on an acute progress, especially when the medulla is affected primarily. These are severe forms, subject to recurrences, and often rapidly fatal. Gilles de la Tourette reports two cases which were cured by the early intervention of energetic specific treatment.

Acute Myelitis.—This is characterized by the sudden onset of acute pain in the dorso-lumbar region, followed in a few days by complete paralysis of the lower limbs, abolition of reflexes, and retention of urine.

Post-mortem changes found in these cases have shown that the process consists in associated myelitis and meningitis, with vascular changes affecting both arteries and veins. The predominance of the meningeal lesions in the region of the posterior nerve roots accounts for the painful phenomena at the onset of the disease. The morbid anatomy is similar in cases of acute and chronic myelitis. In the acute forms the

cell infiltration causes rapid obliteration of the larger arterial and venous vessels, causing necrobiosis of a limited area of nerve tissue. In the forms with slow evolution acute arteritis and phlebitis are replaced by arterio- and phlebo-sclerosis. However, intermediate forms are found between these two types.

Acute myelitis may have a rapidly fatal termination, or may yield to early specific treatment, or may end in chronic myelitis. Gilles de la Tourette reports a case which was cured by antisyphilitic treatment in 1888, and had no further signs when seen in 1893. In cases of acute myelitis which do not end in death or recovery the flaccid paralysis with abolition of reflexes is replaced by spasmodic paraplegia, caused by secondary descending degeneration of the pyramidal tracts. Another point in the symptomatology of syphilitic paraplegia is that the two limbs are seldom affected in the same degree at the same time. This is due to the irregular distribution of the syphilitic lesions.

Chronic Myelitis.—This is the most common form of syphilitic myelitis, and the chief type is that known as the *syphilitic spasmodic spinal paraplegia of Erb*, previously described by Charcot as *syphilitic transverse myelitis*.

It commences with abnormal sensations of numbness and tingling in the feet and legs, followed, after some months or years, by affections of the bladder and rectum. Sometimes there is incontinence of urine, sometimes retention, accompanied by constipation and loss of sexual power. The disease may be arrested at this stage, and Erb states that this form of myelitis has a tendency to spontaneous improvement.

More often, however, in the absence of early treatment, the disease progresses. The lower limbs are affected with painful cramps, and soon lose their usual agility. The knee-jerks and paresis are more marked on one side than the other. The muscles preserve their normal volume and muscular power, in spite of the relative weakness in locomotion, which is due to momentary rigidity whenever movements are attempted. Anæsthesia or hyperæsthesia occur in irregular patches, and tactile perception is often retarded. The irregular distribution

of these phenomena is due to the irregular nature of the spinal and meningeal lesions.

In the clinical type established by Erb the localization of the lesion was always dorso-lumbar, and the upper extremities and the cranial nerves were never affected. Gilles de la Tourette, however, points out that in some cases which correspond to this type of paralysis the upper limbs may be affected; also that changes in the pupil are not uncommonly observed. He states that unilateral myosis and diminution of the palpebral fissure may occur from implication of the communicating branch of the first dorsal nerve with the sympathetic, which contains the dilator fibres of the iris, in the syphilitic lesion. If this localization appears too high for an affection which usually affects the dorso-lumbar region, it must be remembered that if the naked-eye changes are especially marked in the dorso-lumbar region, microscopic examination shows that they extend nearly always to the whole extent of the spinal cord. 'Relative generalization is the rule, as in all syphilitic myelitis, which, especially when it affects a chronic form, is always more or less diffuse.'

The evolution of syphilitic paraplegia is essentially chronic, but the spasmodic paralysis is seldom so complete as to render locomotion impossible and confine the patient to bed. Moreover, the disease may be arrested in its evolution, and even retrogress to a certain extent. The reflexes, however, remain exaggerated, and even if incontinence or retention of urine have disappeared, there remains an urgent desire to micturate. A certain number of these cases, in which the disease has become arrested, may resume their ordinary life; but the greater number, in the absence of early treatment, become incurable paralytics.

Irregular Forms of Myelitis.—Apart from the well-marked types of syphilitic myelitis, there occur irregular forms, characterized chiefly by *muscular atrophy*. Sometimes the atrophy affects the arms or forearms, especially the thenar and hypothenar muscles. The clinical appearance is then that of hypertrophic cervical pachymeningitis, which we have previously considered. At other times the atrophy is

limited to the lower limbs, and accompanied by shooting pains; and in these cases disseminated gummata are found in the cord and meninges. In other cases, however, the atrophy affects the muscles of the upper and lower extremities and the trunk, and resembles the type of *progressive muscular atrophy* of Duchenne. But in these cases the muscular atrophy is a superadded phenomenon accompanied by other signs, such as true paralyses and sensory disturbances, which do not occur in progressive muscular atrophy of the type of Duchenne. The coexistence of diplopia, vertigo, incontinence or retention of urine, with muscular atrophy, is sufficient to establish a diagnosis of syphilis, which is the only disease capable of producing such lesions.

'Disorders of sensation, paralysis of the sphincters, and ocular phenomena, are not the usual appanage of the three great groups of amyotrophy with which we are acquainted: anterior poliomyelitis, amyotrophic lateral sclerosis, and progressive muscular atrophy; but these phenomena are rarely wanting in muscular atrophy due to syphilis. And if syringomyelia is eliminated, the diagnosis is sometimes corroborated by treatment, the action of which, although often limited, is always much more marked than in systematized myelitis or protopathic amyotrophy, in which treatment of any kind is nearly always powerless' (Gilles de la Tourette).

The possibility of the syphilitic origin of other types of spinal paralysis is discussed in the next chapter.

Peripheral Neuritis.—Syphilis may also be a cause of peripheral neuritis. Gilles de la Tourette mentions the case of a woman who suffered from peripheral neuritis affecting all four limbs, fifteen months after infection. The symptoms consisted in dropped feet and atrophy with reaction of degeneration in the extensor muscles. In this case, which was at first thought to be alcoholic peripheral neuritis, the diagnosis was complicated by the fact that the patient had been energetically treated with mercury. Cases of peripheral neuritis due to mercurial poisoning have been recorded by Spillmann and Etienne, but are rare apart from other signs of mercurialism.

The case in question recovered under the administration of iodides.

The Cerebro-spinal Fluid.

In its normal state the cerebro-spinal fluid is clear and free from corpuscular elements. Widal and others have shown that leucocytosis of the cerebro-spinal fluid is one of the earliest signs of organic disease of the nervous system, and that it occurs in tuberculous and syphilitic meningitis, tabes, general paralysis, and multiple sclerosis. On the other hand, leucocytosis is absent in functional neurosis. This leucocytosis is supposed to be a reaction in response to the escape of the products of degeneration into the cerebro-spinal fluid.

Ravaut has shown that in acute and chronic meningitis the cellular elements in the cerebro-spinal fluid are proportional to the degree of intensity of the inflammation, and he states that the condition of the meninges in syphilis may be determined by cyto-diagnosis of the cerebro-spinal fluid obtained by lumbar puncture. This proceeding is therefore a valuable aid in the diagnosis of early causes of syphilitic cerebral disease, and many lesions with no clinical symptoms may be revealed by lumbar puncture. He therefore advocates lumbar puncture in all cases of syphilis with nervous symptoms, the presence of lymphocytosis being an indication for energetic treatment. The degree of lymphocytosis is greater in early than in late cases of syphilis, and in old syphilitics with no manifestations the cerebro-spinal fluid is normal. It is also found to be normal in tertiary syphilis of the skin and bones. In ocular syphilis there is lymphocytosis in early lesions, but not in atrophic cases.

Milian found lymphocytosis in cases of syphilis with headache, but not in cases of headache due to hysteria, neuralgia, or periostitis. The presence of lymphocytosis in cases of syphilitic headache, therefore, points to meningitis.

Widal reports an interesting case of meningitis in a man aged twenty-nine in which there were no signs or history of syphilis, but lymphocytosis was found by lumbar puncture. Injection of the cerebro-spinal fluid into the guinea-pig proved

negative for tuberculosis. The patient recovered under injections of biniodide combined with iodide of potassium. In this case the meningitis was probably syphilitic. Widal also mentions a case of lymphocytosis in syphilis in which meningitis was found at the autopsy. He remarks that in secondary syphilis with no nervous symptoms the virus may in certain cases cause slight meningeal reaction, which can only be demonstrated by lumbar puncture. The meningeal reaction in syphilis varies in intensity, sometimes being as great as in tuberculous meningitis. In enteric fever, on the other hand, the reaction is absent, even if meningeal symptoms are present.

Lymphocytosis, according to the investigations of Babinski and Nageotte, appears to be constant in cases of tabes and general paralysis, and to be present with the Argyll-Robertson pupil in cases in which other symptoms are absent. In some cases the lymphocytosis preceded the pupil phenomenon. These observers also report cases of syphilitic hemiplegia, paraplegia, and progressive muscular atrophy in which the Argyll-Robertson pupil was found associated with lymphocytosis.

Ravaut concludes that 'in a syphilitic all cytological reaction of the cerebro-spinal fluid, either isolated or accompanied by other syphilitic manifestations, is an indication of a nervous affection . . . the reaction should be considered in syphilitics as a symptom as characteristic as a cutaneous or visceral lesion, and bears the same therapeutic indications.' He therefore advocates the systematic practice of lumbar puncture in all cases of syphilis, since by this means the presence of lymphocytosis may indicate active treatment, and prevent the further evolution of organic nervous disease.

Technique of Lumbar Puncture.—This operation consists in tapping the subarachnoid space below the fourth lumbar vertebra—*i.e.*, below a line joining the iliac crests. The skin having been disinfected in the usual way, and the patient lying on one side with the knees drawn up and the spine flexed as much as possible, a point is chosen between the laminæ of the fourth and fifth lumbar vertebræ about an inch from the middle line. The laminæ being imbricated, the direction of

puncture should be slightly inwards and upwards. The exploring needle, previously sterilized, should be $3\frac{1}{2}$ inches long for an adult, and about 2 inches for a child. As the lumbar region is not very sensitive, no anæsthetic is usually required.

Changes in the Pupil.

The researches of Babinski and Charpentier have shown that loss of pupillary reflex to light constitutes by itself a sign which is almost pathognomonic of a syphilitic lesion of the nervous centres. Their conclusion is as follows: 'Abolition of the pupillary reflexes, and more especially that of the reflex to light, when it is permanent and when it is the expression of a lesion limited to the apparatus of pupillary reflexes—that is to say, when it is not connected with any alteration in the globe or the optic nerve, and when it is not associated with paralysis of the third pair—constitutes a sign of acquired syphilis or hereditary syphilis almost, if not quite, pathognomonic.'

Thus the Argyll-Robertson pupil is not the only pupillary sign of syphilis; abolition of the reflex to light, with or without preservation of accommodation, with or without myosis, is by itself a sign of syphilis of the nervous centres.

It appears that in all cases of absence of the reflex to light, even when it is the only sign of nervous disorder, there is lymphocytosis of the cerebro-spinal fluid. Lymphocytosis is the more frequent phenomenon, but is not characteristic; absence of reflex to light is less common, but is almost pathognomonic; both signs together are conclusive.

Therefore, the presence of immobility of the pupil to light, especially when associated with lymphocytosis of the cerebro-spinal fluid, is of the greatest importance in the early diagnosis of cerebral syphilis, since it allows treatment to be begun at a time when it may be efficacious.

Treatment of Cerebro-spinal Syphilis.

The treatment of syphilis of the nervous system must be instituted in the early stages of the disease to give satisfactory

results. Unfortunately, the early symptoms are often vague and indefinite, and the disease is often far advanced before it is diagnosed. Treatment begun during the premonitory stage may save the patient from paralysis, but no amount of mercury or iodide can have any effect on a patch of sclerosis, neither will it restore the function of a vessel which has become blocked by thrombosis. It may arrest the syphilitic process, and prevent further mischief, but it cannot create new nerve cells or nerve fibres, when once these have been destroyed. It is therefore of the greatest importance to pay attention to the early signs of disease of the brain and spinal cord, especially with regard to severe nocturnal headaches, exaggeration of reflexes, and disorders of sensation in the limbs, such as numbness and tingling in the legs, etc. One of the most important signs is abolition of the reaction of the pupil to light, which is by itself an indication for intensive antisyphilitic treatment.

The effect of treatment depends on the age, degree, and extent of the lesions, rather than on the presence or absence of any particular symptom.

With regard to the duration of treatment, Gowers has drawn attention to the fact that treatment may lose its power if continually administered. He holds that after a course of eight weeks' treatment the specific process is at an end, and all that remains is due to the secondary effects. Gowers, therefore, agrees with Fournier in adopting an intermittent form of treatment, and advises 'that specific treatment should be energetic, brief, renewed, but not continuous. It should stop at the end of eight weeks or so, and be renewed after two, four, or six months, and the patient should have three or four weeks' treatment with iodide every four months during the first year after each true specific symptom, and every six months for the next three or four years.'

Gowers also points out a possible effect of treatment which is not well recognised—viz., that treatment, by promoting cicatricial changes in the tissues, may cause constriction of vessels and nerves, and increase the effects of the original disease. In such an event, treatment may be pushed to no purpose as long as symptoms exist.

Another point, mentioned by Hughlings Jackson, is the fallacy of the apparent beneficial effect of treatment in certain cases of cerebral paralysis. He remarks, 'It must never be forgotten that hemiplegia, after a convulsion due to organic disease of the brain's surface, such as syphilitic gumma, is nearly always transitory. Unless there be a repetition of the convulsion, the hemiplegia will pass off in a few hours or days, sometimes leaving the side affected a little weak, although not obviously paralyzed. So, then, if the patient took drugs, an inexperienced person might suppose that he had cured his patient of syphilitic hemiplegia. There are cases in which absolute paralysis, after a convulsion, will pass off in a few hours.' It therefore appears that some of the miraculous effects of treatment which are reported from time to time may be instances of *post* but not *propter hoc*.

The latest scheme for the treatment of syphilis of the nervous system is that suggested by Fournier at the recent discussion on general paralysis at the Paris Academy of Medicine. In this scheme the duration of treatment is extended so as to include the period at which general paralysis occurs with the greatest frequency—viz., the seventh or eighth year, during which an extra course is given. This point will be referred to again in dealing with the general treatment of syphilis.

As regards the methods of administration of antisyphilitic treatment in cerebro-spinal syphilis, most authorities agree that an energetic course of mercurial treatment is essential, either by means of inunction or injections. It is also generally agreed that iodides should be administered concurrently. Considering that the patient in such cases is generally laid up in bed, or, at any rate, confined indoors, dissimulation is unnecessary, and recourse should be had to inunction. If the patient is comatose, or unable to retain medicine, iodide may be given by enemata. The dose of iodide in these cases should be not less than 15 grains thrice daily, and the dose may be increased gradually to 30 grains (Fournier). After an attack of cerebral or spinal syphilis, intermittent treatment should be continued for two or three years.

According to Fournier, the epileptic form of cerebral syphilis is the most amenable to treatment, and treatment during the epileptic stage, before the development of other cerebral complications, is frequently successful. An epilepsy dating for a year or more is still amenable to treatment, provided it is not complicated by other important cerebral symptoms. On the other hand, epilepsy associated with psychic disorders, paresis or paralysis, amblyopia or disorders of speech, is usually incurable. Ripoll cured a case of heredo-syphilitic epilepsy of ten years' duration with mercury and iodides.

As auxiliary therapeutic agents in the epileptic form of cerebral syphilis, Charcot and Fournier recommend hydrotherapy, including a daily cold douche, and bromides combined with the iodide. In cases of mental excitement, however, the cold douche is not recommended. Bromide of camphor is useful in delirium, headache, and insomnia.

It is hardly necessary to add that the patient should avoid excesses of all kinds, both mental and bodily, and should abstain altogether from alcoholic drinks.

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CHAPTER XII

PARASYPHILIS OR QUATERNARY SYPHILIS OF THE NERVOUS SYSTEM

ALTHOUGH there is probably no sharply-defined pathological distinction between parasyphilitic and syphilitic affections, nevertheless, for clinical purposes it is useful to retain the term parasyphilis, or, better, quaternary syphilis, to designate certain postsyphilitic affections which differ in their evolution from the usual manifestations of syphilis. The chief of these affections are tabes dorsalis, general paralysis, and epilepsy; and probably other affections of the nervous system of obscure etiology come under the same category.

Tabes and General Paralysis.

According to Fournier, Ferrier, and Mott, tabes and general paralysis are pathogenically identical, and 'merely different aspects of the same polymorphic disease' (Ferrier). Both affections are caused by syphilis, and both appear about the same time after infection, usually between the sixth and twelfth years. Tabes and general paralysis are sometimes combined or succeed one another in the same individual. The Argyll-Robertson pupil and lymphocytosis of the cerebro-spinal fluid are common to both diseases. According to Ferrier, Gowers, and Mott, the primary lesion in both tabes and general paralysis is a dystrophy of the neurones and their connections, the sclerosis and thickening of the membranes being a secondary result of parenchymatous degeneration. Ferrier suggests that the terms cerebral tabes, spinal tabes, and cerebro-spinal tabes should be substituted for general paralysis, locomotor ataxy, and tabo-paralysis.

Tabes.

The syphilitic origin of tabes was first pointed out by Fournier in 1875, later on by Gowers and Erb, and is now generally accepted. Erb established evidence of syphilis in 90 per cent. out of 1,100 cases of tabes occurring in patients of the better class; whereas out of 10,000 cases of other diseases, excluding tabes, in the same class of patient, there was evidence of syphilis in only 21 per cent. Therefore, evidence of syphilis was found four or five times more often in tabetics than in other patients. It has been shown that evidence of syphilis can only be obtained by careful examination in about 80 per cent. of cases of obvious syphilis of the skin (Pernet), and this will account for the absence of syphilitic antecedents in the remaining 10 per cent. of cases of tabes (*syphilis ignota*). Tabes may therefore be regarded as certain evidence of syphilis (Ferrier).

Tabes usually occurs between the ages of thirty and forty, but may appear in advanced age. Berger records a case of tabes in a man of seventy-four who contracted syphilis at the age of seventy. It is less common in women than in men, thus differing from juvenile tabes, which is equally common in both sexes, whether caused by hereditary syphilis or acquired syphilis in infancy.

Conjugal tabes is not uncommon, and there is almost always a history of syphilis on one side. Nonne records the case of a child, aged five years, who was infected with acquired syphilis and became tabetic at the age of eighteen. This child infected its mother, the latter infected the father, and both became tabetic. Souques reported the history of a family in which the father was syphilitic and became a general paralytic; the mother was tabetic, and two daughters developed tabes.

An argument which is sometimes raised against the syphilitic origin of tabes and general paralysis is its alleged rarity among certain races who suffer from syphilis (Bosnia, Abyssinia, Arabs, negroes, etc.). This, however, appears to be a fallacy, for it has been stated that tabes is common in Bosnia

and Abyssinia, and occurs among negroes. As Ferrier remarks, 'if tabes can be shown to exist or to have existed in any land or people among whom syphilis has never entered, and who have never had any communication with any outside syphilized world, the exclusively syphilitic origin of tabes will have to be abandoned, but not till then.'

Accessory Causes.—Other causes no doubt contribute to the development of tabes, but undue importance has been attached to sexual excess, exposure to cold, and 'neuropathic heredity.' However, certain families appear to be more liable to tabes than others. Fatigue and over-exertion, both mental and bodily, are accessory causes when they act on a soil prepared by syphilis. The parts subjected to the greatest strain give way, such as the sensory apparatus concerned in co-ordinated locomotion and the maintenance of equilibrium. This may explain the incidence of tabetic degeneration on the brain in one case and the spinal cord in another. Raymond reported the case of two brothers who were both infected with syphilis at the same age: one had led a fast life, and became tabetic; the other exhausted his brain and developed general paralysis.

Morbid Anatomy.—The macroscopic changes consist in thickening of the pia-arachnoid over the posterior surface of the cord, and atrophy of the posterior roots and columns, which are of a gray colour. The changes are most marked in the lumbar region, but in some cases (cervical tabes) the cervical region is affected. In early cases the area of degeneration is limited to the middle third of the posterior columns, but in advanced cases most of the posterior columns become degenerated, with the exception of the endogenous fibres. 'The essential morbid change in tabes is confined to the elements of the sensory or afferent neurones, the up-bearing neurones, dependent on the posterior ganglia. The motor neurones—the motor cells and fibres—are never altered in pure tabes' (Gowers).

The histological changes consist in breaking up of the myelin sheaths, irregularity or atrophy of the axis cylinders, and increase of the neuroglia. According to Ferrier, there are no active vascular changes present.

Pathogeny.—According to Nageotte and other observers, tabes begins as a *syphilitic meningitis*, which implicates the posterior roots at their points of emergence from the dura mater, and is followed by a neuritis and secondary degeneration of the posterior roots. The early occurrence of lymphocytosis of the cerebro-spinal fluid is urged in support of this view. Other neurologists, including Ferrier, Gowers, and Mott, regard both tabes and general paralysis as due to primary degeneration of the neurones.

The *objections to the meningeal theory* are—(1) meningitis is not constant in tabes; (2) intramedullary degeneration is often well marked when the posterior roots show no changes; (3) the escape of the anterior roots is difficult to explain. 'The symmetrical and segmental characters of the tabetic degenerations, which it would be difficult to correlate with any, so to speak, brutal meningeal inflammation, and the occurrence of degenerations elsewhere, such as in the optic nerve, ciliary ganglion, and sympathetic system, are all formidable arguments against the meningeal origin of tabes' (Ferrier).

Lymphocytosis has been shown by Widal, Ravaut, and Sicard to occur in the earliest stages of tabes and general paralysis, and may occur before any changes in the pupil. This has been put forward as evidence in support of the meningeal theory, but lymphocytosis occurs in other affections without meningitis, syphilitic or otherwise—for instance, Landry's paralysis, pernicious anæmia, and herpes zoster. Hence lymphocytosis cannot be regarded as pathognomonic of meningeal inflammation.

Ferrier adduces the fact that tabes and general paralysis do not react to antisyphilitic treatment as an argument against their syphilo-meningeal origin; but it is seldom that treatment is instituted in the earliest stages, and the later stages of the disease come under the category of parasyphilis, which does not react to specific treatment.

The Dystrophic Theory.—Ferrier adopts the view 'that the essential lesion of tabes is a dystrophy, similar to that induced by certain toxic agents, affecting the sensory proto-neurone as a whole, and manifesting itself in degeneration

both of the peripheral and central terminations, of which the intramedullary are the most vulnerable, and are usually the earliest to exhibit anatomical change. The process, however, is not confined to the spinal protoneurone, but may affect, among others, the optic, the sympathetic, and certain motor neurones.'

The sensory neurones and posterior columns appear vulnerable to certain toxic agents; for example, the ataxic symptoms which occur in ergot-poisoning, which are due to degenerative changes in the posterior roots and columns similar to those of tabes. Alcohol, lead, and arsenic, which cause peripheral neuritis, also sometimes give rise to degeneration of the posterior roots and columns. Many organisms, such as those of lepra, diphtheria, and beri-beri, generate toxins which have the same effect on the peripheral nerves and posterior columns. Again, in pernicious anæmia and diabetes degenerations occur in the cord, with pseudo-tabes.

All these facts are urged by Ferrier in support of the toxic origin of tabes, and he concludes that the most probable pathogeny of the tabetic degeneration is a toxin generated by the syphilitic micro-organism. This view, he admits, is open to the objection that it is difficult to conceive a toxin lying dormant for such a long time, and afterwards giving rise to the tabetic process, which would imply a progressive and continuous generation of the poison. Ferrier suggests that the syphilitic virus, under certain conditions, may affect some gland of the organism, so that it elaborates an internal toxic secretion which acts on the nervous system.

Gowers also adopts the view that tabes is caused by a nerve poison generated by the syphilitic virus, and states: 'We must certainly regard the disease as one capable of giving rise to a toxin, and tabes as such a disease as a toxin might cause. But all other known toxins of specific disease are produced during the active stage of the malady, and their influence is exerted speedily, endures for a time, and then ceases. This sequel (tabes) occurs, as a rule, years after the last manifestation of active syphilis. It develops and varies without relation to any condition to which it can be referred.

Tabes behaves as if it were an absolutely random malady—unconditioned, irresponsible. Its course is so erratic that a forecast cannot be made with certainty in any individual case. Its first symptoms may remain for ever trifling, or may remain stationary for years, and then steadily increase; or they may develop from the first, and steadily reach a high degree; or a stationary period may undergo an increase so rapid as to attain in a few days a degree usually only reached after many months. The onset or increase of the disease bears no relation to any evidence of activity of the preceding syphilis. Although years have commonly elapsed since the last constitutional symptoms, occasionally tabes develops before the constitutional malady has ceased. Then the degenerative change is found coexisting with true specific lesions. Moreover, no treatment of the primary disease certainly prevents the occurrence of tabes.

'We cannot explain the mystery by conceiving that an early toxin simply lessens the vital endurance of the nerve elements; the facts of rapid development or rapid increase, even after years, compel the conviction that the morbid agent is present at the time. Equally incompatible with the theory of lessened vital endurance is the remarkable degree of recovery sometimes met with, even in characteristic cases. We cannot conceive that syphilis, although it is doubtful what immunity follows an attack, may yet cause a change in chemical processes which results, after years, in the generation of a nerve poison. The neurotoxic effect of the exciting cause of tabes may depend on more than one agent co-operating with that which follows syphilis.'*

* Another theory has recently been promulgated by Ford Robertson, who holds that general paralysis is the result of a bacterial toxic infection from the respiratory and alimentary tracts caused by the *Bacillus paralyticans*, which acts on an organism impaired by syphilis, alcohol, and excess of nitrogenous food. He attributes the lesions of the cord in tabes to the absorption of toxins from septic foci in the bladder, etc. However, according to Bulloch, the *Bacillus paralyticans*, which resembles the Klebs-Loeffler bacillus, does not differ from other diphtheroid organisms which are commonly found both in health and disease. Bulloch failed to find this organism in the cerebro-spinal fluid, blood, and urine in cases of tabes and general paralysis, so that the *Bacillus paralyticans* is probably accidental.

Pathological Physiology.—The chief signs of tabes are lightning pains in the limbs and the so-called 'gastric crises'; loss of knee-jerk; inco-ordination of movement, without loss of muscular power, producing the ataxic gait; inability to stand with the feet together and the eyes shut (Romberg's sign); inability to stop and turn round suddenly when walking; loss of pupil reflex to light, with preservation of accommodation (Argyll-Robertson pupil); genito-urinary disorders, and osteo-arthropathy.

Babinski has drawn attention to loss of the ankle-jerk as an early sign of tabes, and states that it may occur before the loss of knee-jerk. Abadie also mentions analgesia of the tendo Achillis as another early phenomenon.

Lightning Pains.—Sir William Gowers has recently drawn attention to the pains of tabes, which he says are more common than ataxy, begin earlier, and may constitute the only sign of the disease. These pains, which are often mistaken for rheumatism, are momentary and paroxysmal, and recur in the same place.

They may be superficial or deep, and the former cause intense tenderness of the skin, even in parts where sensibility to pain is lost. Sensibility to touch in tabes is less often lost than to pain.

In addition to the lightning pains, there occur prolonged pains, especially in the epigastric region, and often unilateral (girdle pains). These may be mistaken for intercostal neuralgia or renal colic. Sometimes there is pain along the course of the sciatic nerve, which is probably due to actual sciatic neuritis. A common form of pain is referred to the tendons of the hamstring muscles, or in the calf or sole. This pain may be very severe, and last for twenty-four to forty-eight hours, with occasional exacerbations. Another form consists in tingling and numbness, which may last for weeks or months.

Tabetic Neuralgia.—This is a form of tabes manifested by pains only, without loss of knee-jerk or ataxy. It may remain in the same condition for years, and is regarded by Gowers as a variety of tabes, and not as a stage in the development of the disease. It is usually associated with changes in the

pupil. The pains in such cases are usually attributed to rheumatic gout or to neuritis, 'which has become a frequent diagnostic refuge.' Pains due to other causes may resemble the deep pains of tabes, but momentary, stabbing, 'lightning' pains are characteristic of tabes.

Cases of tabetic neuralgia have a better prognosis than others, and, according to Gowers, the danger of ataxy is small. Gowers regards the pains of tabes as due to changes in the nerve-endings in the sheaths of the nerves, Ferrier to changes in the posterior roots.

Ataxia.—Tabetic ataxia is due to loss of centripetal impressions of all kinds, conscious or unconscious, those from the muscles, tendons, and joints being more important, and travelling by the afferent fibres in motor nerves discovered by Sherrington. Inco-ordination is worse in the absence of vision, which has a compensatory action; hence the tabetic symptoms are worse when the eyes are shut. A characteristic feature of tabetic movements is over-action of the principal muscles, owing to defective sense of the movement achieved.

Ataxy, although the most characteristic feature of tabes, may be absent, and a tabetic patient may become blind from optic atrophy, or suffer for a long time from lightning pains or genito-urinary troubles without becoming ataxic.

Loss of Knee-jerk.—Wherever there is marked ataxy, the sensitiveness of the muscles is diminished or absent. This explains the loss of knee-jerk. 'The tap on the tendon excites a local muscular contraction, but the local excitability of the muscle is due to its tone, augmented by the gentle tension necessary for the mechanical stimulus to act on it. If a tendon is rigidly fixed, so that the tap on it does not act on the muscle, no contraction results. It is the excitability of the muscle that is reflex, and is dependent on the spinal cord; it is really identical with muscle tone. Its loss is a delicate indication of the impairment of the afferent muscle nerves, shown later by the loss of muscular sensibility' (Gowers). Loss of knee-jerk always precedes ataxia.

Osteo-arthropathy.—Tabetic osteo-arthropathy, or Charcot's joint disease, occurs in tabes, but is infrequent. It

usually affects one of the knee or ankle joints, less commonly the hip, elbow, shoulder, wrist, and vertebral column. There is usually much swelling of the joint, due chiefly to enlargement of the ends of the bones and partly to effusion. The peri-articular tissues are thickened by a kind of hard œdema; the cartilages are eroded, causing grating on movement; and osteophytic growths are usually present. The condition of the joint, therefore, resembles that of rheumatoid arthritis, but dffers in usually affecting one joint only, and in the absence of pain, which is a characteristic feature of all tabetic dystrophies. In tabes sensation to pain is lost before sensation to touch. The bones become rarefied and less opaque to the X rays, and the surfaces become worn down when the cartilage has eroded away. Subluxation is common: backwards in the case of the tibia, upwards in the case of the femur.

The dystrophic effects of tabes are usually attributed to disorder of the 'trophic nerves,' but Gowers points out that there is no evidence of the existence of such special nerves, and he regards the dystrophies as due to an altered state of nutrition of the ordinary sensory nerves, which disturbs the vitality of the tissues themselves.

PERFORATING ULCER OF THE FOOT is another dystrophy met with in tabes and other nervous disorders (syringomyelia, etc.), and usually starts from some slight injury, such as cutting a corn. Owing to the absence of pain, the lesion causes little attention, and the normal process of healing is defective from the altered condition of the sensory nerves. It is the absence of pain which leads the patient to neglect these dystrophic lesions till they have progressed too far to be dealt with by the usual methods of treatment.

Treatment.—According to most authorities, mercury and iodides have no effect on the progress of tabes, and some go so far as to say that severe mercurial treatment aggravates the disease. On the other hand, cases have been reported in which improvement or arrest of the disease is said to have followed intensive mercurial treatment by injections in the early stages of the disease.

It must be borne in mind that tabes is sometimes arrested spontaneously, and this may explain some of the 'cures' which were attributed to mercury. Both Gowers and Ferrier are of opinion that, although antisyphilitic treatment may improve coincident tertiary lesions or cure pseudo-tabetic symptoms, it has no effect on the tabetic degeneration.

For the pains of tabes Gowers recommends antifebrin, antipyrin, and phenacetin, and also chloride of aluminium in 5 to 10 grain doses thrice daily. In severe cases injections of cocaine may be used.

The best general treatment for tabes appears to be the system of re-education of the muscles advocated by Fraenkel, combined with general hygienic measures.

General Paralysis.

The relationship of general paralysis to syphilis has been the subject of a recent discussion at the Paris Academy of Medicine (February and March, 1905). As this debate contains all the arguments *pro et contra*, expounded by some of the most eminent authorities, it will be well to give a full abstract thereof.

Fournier reported 112 cases in which the date of the chancre and the date of the cerebral affection were established beyond doubt, showing the date of appearance of general paralysis.

The results of these cases are shown as follows:

Towards the end of the third year	1 case
In the course of the fourth year	3 cases
,, ,, sixth ,, ...	7 ,,
,, ,, seventh ,, ...	8 ,,
,, ,, eighth ,, ...	10 ,,
,, ,, ninth ,, ...	10 ,,
,, ,, tenth ,, ...	15 ,,
,, ,, eleventh year	12 ,,
,, ,, twelfth ,, ...	11 ,,
,, ,, thirteenth year	5 ,,
,, ,, fourteenth ,, ...	7 ,,
,, ,, fifteenth ,, ...	6 ,,
,, ,, sixteenth ,, ...	2 ,,
,, ,, seventeenth ,, ...	2 ,,

In the course of the eighteenth year	... ...	5 cases
,, ,, nineteenth ,,	... ...	3 ,,
,, ,, twentieth ,,	... ...	2 ,,
,, ,, twenty-third year	... ...	2 ,,
,, ,, twenty-fourth year	... ...	1 case
Total	... ...	112 cases

These figures show (1) that general paralysis is unknown in the first two years of syphilis; (2) that its earliest appearance is in the course of the third year; (3) that it is rare before the sixth year; (4) that it most commonly occurs between the sixth and twelfth years, with a maximum at the tenth year; (5) that it becomes progressively less frequent after the thirteenth year.

The percentages are thus:

In the two first years	0
From the third to the fifth year	3·5
From the sixth to the twelfth year	65·4
From the thirteenth to the twentieth year	28·5
Beyond the twentieth year	2·6

Hence about four-fifths of the cases occur from the sixth to the fifteenth year, with a maximum for the tenth (81 per cent.).

These figures differ considerably from those showing the date of onset of ordinary cerebral syphilis. For comparison Fournier gives the figures of 228 cases, showing the date of onset of syphilitic hemiplegia, the most common and best-defined type of cerebral syphilis.

First year	25 cases
Second year	26 ,,
Third ,, ...	39 ,,
Fourth ,, ...	29 ,,
Fifth ,, ...	20 ,,
Sixth ,, ...	10 ,,
Seventh ,, ...	13 ,,
Eighth ,, ...	4 ,,
Ninth ,, ...	6 ,,
Tenth ,, ...	5 ,,
Eleventh year	4 ,,

Twelfth year	5 cases
Thirteenth ,, ...	3 ,,
Fourteenth ,, ...	4 ,,
Fifteenth ,, ...	4 ,,
Sixteenth ,, ...	1 case
Seventeenth ,, ...	3 cases
Eighteenth ,, ...	1 case
Nineteenth ,, ...	5 cases
Twentieth ,, ...	3 ,,
Twenty-first ,, ...	1 case
Twenty-second year	5 cases
Twenty-third ,, ...	3 ,,
Twenty-sixth ,, ...	2 ,,
Twenty-seventh ,, ...	1 case
Twenty-ninth ,, ...	1 ,,
Thirtieth ,, ...	2 cases
Thirty-third ,, ...	1 case
Thirty-fourth ,, ...	1 ,,
Fortieth ,, ...	1 ,,

Thus in cerebral syphilis two-thirds of the cases occur in the first six years of the disease; while in general paralysis about two-thirds of the cases occur between the sixth and twelfth years of the disease.

As regards the *etiology* of general paralysis, Fournier recognises syphilis as the constant cause, and alcoholism, nervous overwork, and sexual excess as accessory causes. The subjects of a neurotic temperament and those who lead a life of excitement or of constant vicissitudes are 'candidates for general paralysis,' but in the majority of cases these accessory causes were absent. The so-called 'nervous heredity' plays a very small part in the etiology of general paralysis.

According to Fournier the chief factor in the causation of general paralysis is *insufficient treatment*. General paralysis usually follows benign cases of syphilis, and this probably explains the fact that in the great majority of the cases of general paralysis the antisyphilitic treatment has been insufficient.

In 79 cases in which precise details of the treatment were known, this had been carried out as follows:

4	cases	were treated	for three or four years.
12	,,	,,	two years.
19	,,	,,	one year.
44	,,	,,	six months or less.

Hence four-fifths of the cases had received insufficient treatment, and only 5 per cent. had had what Fournier considers complete—viz., three or four years.

With regard to the mercurial treatment of established general paralysis, Fournier has never seen any benefit from it. The only treatment is *preventive*, by a long course of mercury lasting at least four years in total, but subdivided into several courses, of which the two last are taken at the fifth and again at the seventh or eighth year, *the two periods at which general paralysis is most likely to occur.*

Fournier's new method, which he terms the *method of mercurial treatment at late periods*, comprises :

1. Thorough treatment for the first two years, carried out by the chronic intermittent method with intervals of rest.
2. A rest of two years.
3. A year's treatment during the fifth year.
4. A year's treatment at the seventh or eighth year.

Fournier compares the action of mercury to vaccine, which is a preventative for a certain time. In the same way that revaccination is necessary to acquire prolonged immunity, so is remercuralization required for syphilis. An illustrative example of this is shown by the possible alternations of healthy and diseased pregnancies in a syphilitic couple, according to the intervention or non-intervention of treatment.

In addition to the long mercurial treatment, special attention must be given to general hygiene, and all overwork of the nervous system, both cerebral and spinal, must be avoided as far as possible. Hydrotherapy is especially beneficial.

Raymond agreed with Fournier in the importance of syphilis as a cause of general paralysis; in the date of appearance of the latter in relation to syphilitic contamination ; in its occurrence after apparently benign syphilis, and especially after insufficient treatment ; lastly, in the failure of antisyphilitic treatment. But he attached more importance to the influence of heredity,

which also plays an important rôle in the pathogeny of tabes. General paralysis is usually developed on a soil prepared less by psycho-neuropathic heredity than by heredity of diminished resistance of the cerebral cortex. Those subjects who are predisposed are generally emotional, with vasomotor disorders. Clinical experience shows the frequency, or almost constancy, of syphilis in general paralytics.

Pathological anatomy has also shown, in some cases, the co-existence of characteristic lesions of cerebral syphilis with those of general paralysis in the same brain. These are often only found by cutting a series of sections of the brain, and following all the vessels in the furrows separating the convolutions. Also the preliminary meningitis of both general paralysis and tabes has been proved by the presence of lymphocytosis of the cerebro-spinal fluid (see p. 236).

General paralysis occurring in children, or juvenile general paralysis, is now known as a diffuse meningo-encephalitis. Juvenile general paralysis shows the influence of a preparatory soil, and in this case such causes as alcohol, sexual excess, and overwork can be eliminated. Raymond cited one important case in which the child was the son of a tabetic, and developed syphilitic iritis at the age of seven years.

Raymond concluded that if syphilis and alcohol were suppressed, the majority of nervous diseases, and especially tabes and general paralysis, would disappear.

Joffroy, on the other hand, regarded general paralysis and syphilis as two distinct affections. General paralysis may be seen in the subjects of syphilis, but it is not syphilitic general paralysis. It cannot be denied that syphilis is more frequent in the antecedents of general paralytics than in the case of other insanities; but this only signifies that syphilis favours the development of general paralysis, and not that the latter is necessarily syphilitic. Tertiary lesions are rare in general paralysis; also they are cured by mercury, which has no effect on general paralysis.

The statistics of Fournier showed that general paralysis begins at a variable period in syphilis, usually between the sixth and twelfth years, but also between the third and twenty-

fourth years. As the first phases of general paralysis may pass unperceived, it is possible that, in the cases where it seems to begin at the third year, it has in reality begun at the same time as the syphilis, or even before it.

The influence of the treatment of syphilis on the ulterior development of general paralysis does not seem clear, for there are many cases of general paralysis in which the syphilis has been well treated. In fact, antisyphilitic treatment does not prevent general paralysis any more than it cures it. The former existence of syphilis does not prove that it is the cause of general paralysis, and as this may develop in a non-syphilitic subject, it may also develop in a syphilitic apart from the action of syphilis. Joffroy had never seen mercury cause improvement in general paralysis. He repudiated it both as a curative and as a prophylactic agent, and also regarded intensive mercurial treatment as harmful in such cases.

Lancereaux, who formerly admitted that general paralysis might be syphilitic, now renounces this view. There are cases where syphilitic lesions simulate general paralysis, but the characteristic lesion of diffuse periencephalitis is absent. The criterion of syphilitic manifestations is found only in the macroscopic and histological characters, and in the evolution of the anatomical lesion. The question of the syphilitic origin of general paralysis cannot be settled by statistics, and as there are general paralytics who have never had syphilitic lesions, it follows that general paralysis is not syphilitic.

The tertiary lesions of syphilis are characterized by their circumscribed nature, with a tendency to resolution. On the contrary, the lesions of general paralysis, if they are developed at the expense of the neuroglia and around the small vessels, like those of syphilis, are continuous, and tend towards definite organization, without ever undergoing natural absorption. The absence or rarity of general paralysis in countries where syphilis is common, and the failure of antisyphilitic treatment, support the opinion that general paralysis is not a syphilitic manifestation.

Cornil pointed out the anatomical differences between the lesions of general paralysis and those of syphilis. Gummata

of the brain and meninges, of various sizes, are characteristic in appearance. The same with syphilitic cerebral arteritis. But the lesions of general paralysis are diffuse, and generalized over the pia mater and cerebral cortex of both hemispheres. They are constituted by an infiltration of leucocytes in the perivascular sheaths, and by lesions of the cortex, with disappearance of the myelin of the tangential fibres and atrophy of the nerve cells. The reported cases of the coincidence in the same brain of syphilitic lesions and general paralysis require confirmation. Cornil only recognised syphilis as a factor in the etiology of general paralysis in the same way as intellectual overwork, emotions, or heredity in subjects who have never had syphilis.

Fournier was surprised that the existence of syphilitic general paralysis had been contested. He considered it proved by the following arguments: The great frequency of syphilitic antecedents in general paralytics; the considerable number of syphilitic cases which end in general paralysis; the extreme rarity of general paralysis in women; the relative rarity in the country, in ecclesiastics, Quakers, etc.; the greater proportion of syphilitic antecedents in general paralytics than in other forms of insanity; the common association of general paralysis with tabes; the undoubted existence of a juvenile general paralysis in hereditary syphilis. The last argument is more important than the others, because in these subjects syphilis is the only factor; alcoholism, overwork, and other nervous causes being eliminated by the age of the patients.

The importance of syphilis as the cause of general paralysis is now generally admitted. It remains to be proved if general paralysis can be caused by alcoholism, overwork, or heredity alone.

Lancereaux doubts the value of statistics, but their importance cannot be denied when they show in 90 per cent. of cases the connection between general paralysis and syphilis. Moreover, the proportion of 90 per cent. of syphilitic antecedents in general paralytics is exactly that furnished by antecedents in subjects with undoubted syphilitic lesions, such as gumma of the palate. Hence many regard general paralysis as always of syphillitic origin.

It is not possible to indicate the characters which distinguish syphilitic from non-syphilitic general paralysis, because what has always been described under the name of general paralysis is precisely syphilitic general paralysis. Joffroy denies the prophylactic influence of mercurial treatment on general paralysis, and seems to regard mercurial treatment as favouring the development of general paralysis. Fournier's statistics, however, show that, out of 100 cases of general paralysis observed in syphilitics, 95 occurred in cases which were insufficiently treated and only 5 after proper treatment.

Fournier continues to regard general paralysis as a parasyphilitic affection. Further arguments in favour of this view are the cases of conjugal and consanguineous general paralysis occurring in families; cases of general paralysis developed in subjects infected from the same syphilitic source; the occurrence of undoubted syphilitic lesions accompanying general paralysis; and the existence of the Argyll-Robertson pupil, which Babinski has attached to syphilis.

The pathologists who establish a difference between the lesions of cerebral syphilis and those of general paralysis seem to forget that they do not perhaps yet know all the lesions which may be caused by syphilis, and that they have no right to assign an arbitrary limit to these, confined to what is known at the present day. The arguments which are brought forward in the name of pathological anatomy against the syphilitic origin of general paralysis are exactly the same as were invoked against the syphilitic origin of tabes and leucoplasia.

One cannot argue that general paralysis is not of syphilitic origin because its lesions have not the specific characters of syphilis. Many lesions which have not the typical characters of tubercle are none the less certainly of tuberculous nature.

Conclusion.—From the above evidence we must draw the conclusion that syphilis is the fundamental cause of general paralysis, and that other causes, such as alcoholism, overwork, sexual excess, etc., are accessory causes. The reason why general paralysis is rare in certain countries where syphilis is common no doubt lies in the fact of the absence of these

accessory causes and the different mode of life. Lancereaux's statement that a large number of general paralytics have not had syphilis is absurd, for it is impossible to exclude antecedent syphilis in anyone. Cornil's objection, based on the histological differences between the lesions of syphilis and general paralysis, is also untenable, as Fournier points out; for if the syphilitic origin of a disease is supported by the weight of clinical evidence, the anatomical characters hitherto regarded as characteristic of that disease require revision. The coexistence of typical syphilitic lesions in the brain in cases of general paralysis may be objected to as a coincidence, but is strongly suggestive of the syphilitic origin of that disease.

The negative results obtained by Krafft-Ebing with the inoculation of syphilis in several cases of general paralysis have been objected to because control experiments on healthy persons were not made with the same virus. There is now a possibility of repeating these experiments with monkeys as control cases.

The occurrence of authentic cases of syphilitic chancres in the subjects of general paralysis is no argument against its syphilitic origin, because at the date of the disease at which general paralysis occurs it would be quite possible for reinfection with syphilis to occur.

Morbid Anatomy.—The dura mater is thickened and adherent, and the brain atrophied, especially the frontal and central convolutions. The pia arachnoid is thickened, and the cerebro-spinal fluid is increased in quantity. The lateral ventricles are distended, and the ependyma of all the ventricles is thickened. The brain substance tears away from the membranes, leaving a worm-eaten appearance of the surface. Microscopically, there is thickening of the pia arachnoid and overgrowth of the neuroglia.

Some authorities regard the disease as a primary meningo-encephalitis with secondary atrophy of the nerve elements, but Ferrier, Mott, and others consider the primary change to be a dystrophy of the neurones, in the same way as they look upon the pathogeny of tabes.

Symptomatology.—The result of the cerebral lesions is to cause gradually progressive dementia, owing to atrophy of the association fibres of the brain. In the early stages of the disease the characteristic signs are tremor of the lips, tongue, and hands, slurring speech, unsteady handwriting, grandiose delusions, unequal pupils, and the loss of pupillary light reflex. Lymphocytosis of the cerebro-spinal fluid is also an early phenomenon. In the later stages there is gradual loss of all mental power and voluntary movement.

Ocular Changes in Tabes and General Paralysis.

The Argyll-Robertson Pupil.—In this there is loss of reaction to light, but preservation of the reaction to convergence and accommodation. It is a characteristic and early sign of tabes, and persists during the whole duration of the disease. It is usually bilateral, but may sometimes remain unilateral for a certain time. The Argyll-Robertson pupil also occurs in general paralysis, but then coincides with inequality of the pupils, which is rarely met with in tabes.

Marina has observed degenerative changes in the short ciliary nerves and ciliary ganglion in cases of tabes and general paralysis with Argyll-Robertson pupil, but not in cases with normal pupils. 'There is, therefore, nothing improbable in the assumption that in tabes the ciliary ganglion and ciliary nerves are so affected that, though they cannot transmit the reflex impulse of light to the sphincter pupillæ, they can readily allow the more powerful stimulus associated with accommodation to pass through. It is also probable that the myosis which is so commonly associated with the reflex iridoplegia in the tabetic pupil is due to degenerative changes of an irritative character which are going on in the sphincter' (Ferrier).

Westphal's Sign.—When the pupillary reaction to light and accommodation are absent, after a strong effort to close the eyes, the pupils contract. This peculiarity is especially found in tabes and general paralysis. It has been explained by stimulation of the nucleus of the facial nerve, at the moment

of contraction of the orbicularis muscle, reacting on the nucleus of the oculo-motor.

In tabes there may also be absence of the pupillary reflex to pain, so that when a sensory nerve is stimulated the pupil does not dilate as it does in the normal subject.

Changes in the Form and Size of the Pupil.—Both myosis and mydriasis may occur in tabes and general paralysis, or one condition on each side. It can be determined by local applications whether the myosis or mydriasis are due to stimulation or paralysis of the third nerve or the sympathetic. Myosis in tabes is generally associated with loss of reflex to light. The lesion has been attributed to the cilio-spinal centre, situated at the level of the last cervical and first three dorsal vertebræ. Mydriasis is less common, and often due to stimulation of the cervical sympathetic.

Inequality of the pupils is especially characteristic of general paralysis, but is also common in tabes. It is nearly always associated with loss of the light reflex.

Motor Affections.—Blepharospasm may occur at an early period in tabes, but is usually transient and intermittent.

Paralysis is frequent. More than half the cases of ocular paralysis are of tabetic origin. They occur in all degrees and forms, and may affect all three motor nerves of the eye, the intrinsic and extrinsic muscles, or both together. The third nerve is the most often affected; and, in order of frequency, the internal rectus, inferior rectus, superior rectus, inferior oblique, and levator palpebræ muscles. Paralysis of the facial nerve has been noted, but is rare.

Although these paralyses may be observed at all periods of tabes, they may be divided clinically into those of the preataxic period and the confirmed period.

The *preataxic paralyses* are characterized by being incomplete, dissociated, instantaneous, and transitory. They appear and disappear suddenly, and vary in duration from a few days to several weeks. Deviation of the globe and diplopia vary with the paralysis. The characters of these paralyses show that they are due to peripheral neuritis.

The *paralyses of the confirmed period* differ from the preceding

in their mode of onset, which is generally slow and progressive and more complete. Paralysis generally affects the whole nerve, and even when partial the nerve is profoundly affected. The evolution is progressive and the prognosis bad. The lesion is of nuclear or, more probably, radicular origin.

These forms of paralysis closely resemble the syphilitic paralyses (Chapter XIII.), and may be confounded with them; but there are generally other signs of tabes present, which explain their origin. They may affect any of the extrinsic muscles of the eye, and the ciliary muscle and sphincter of the pupil. Paralysis of accommodation is more common in cerebral syphilis than in tabes.

Diplopia may not be apparent, owing to the frequent coexistence of sensory affections. If one of the eyes is affected with optic atrophy, binocular vision is lost and diplopia does not occur.

Optic Atrophy.—This constitutes, with the motor and pupillary paralyses, a symptomatic triad, or syndrome, which is characteristic of tabes. At least a third of the cases of optic atrophy are due to tabes. It may precede the other signs of tabes, and remain the only sign for ten or twenty years (Charcot, Gowers). Thus in most of the cases of so-called simple atrophy examination at intervals of several years will nearly always reveal the presence of medullary symptoms, which were absent at first.

Optic atrophy occurs in two forms—neuro-retinitis, which is rare, and primary optic atrophy, which is the usual form. This causes slowly progressive changes in the field of vision and in visual acuteness. The two eyes are generally affected at different times. The affection ends in blindness after an interval of three months to six years, the average time being two or three years. An early sign in the diagnosis of optic atrophy is diminution of the field of vision for colours.

General Paralysis.—The frequency of ocular affections in the course of general paralysis is of great diagnostic value. Of all the symptoms of the disease, they are the most clearly marked and the most easy to discover. The psychic disorders are not always sufficiently characteristic—at any rate, at the

onset of the disease—to affirm the diagnosis. The ocular symptoms, together with lymphocytosis, are the most constant signs of general paralysis.

The ocular manifestations of general paralysis are the same as those of tabes, and only differ in degree of frequency. The most constant are the pupillary affections; next in order of frequency are changes in the papilla; and the least common are muscular paralyses.

Reflex to Light.—In more than half the cases the reflex to light is abolished or diminished, while accommodation is preserved (Argyll-Robertson pupil). As in tabes, this affection is bilateral, but the two eyes may be unequally affected. The sign of Argyll-Robertson persists indefinitely, and, as in tabes, remission is exceptional. Accommodation is less often affected, but it is also sometimes lost, constituting ophthalmoplegia interna.

The Pupil.—Inequality of the pupils occurs in more than half the cases, and when occurring in a syphilitic subject should suggest the onset of general paralysis. Sometimes there is bilateral myosis or mydriasis, or the pupil may be irregular in shape—oval, triangular, or quadrilateral.

According to Babinski, Joffroy, and others, every change in form of the pupils—congenital abnormalities and synechiæ excepted—is pathognomonic of syphilis, general paralysis, or tabes, even if the light reflex is retained; and the diagnostic value of irregularity of the pupil is equal to that of the Argyll-Robertson pupil, which it often precedes. Piltz has produced irregularity of the pupil in dogs by stimulation of the long and short ciliary nerves.

Optic Atrophy.—This is generally incomplete, probably owing to the rapid evolution of the disease. When complete, it has the same characters as in tabes. It rarely ends in complete blindness, because the patient generally dies first.

Heredo-parasyphilis.

Under this term may be placed cases of heredo-syphilitic tabes, general paralysis, epilepsy, and possibly other nervous disorders of obscure etiology.

Heredo-syphilitic Tabes or Juvenile Tabes.—The recognition of tabes of heredo-syphilitic origin is of comparatively recent date, but was established by Fournier in 1886. Babinski in 1902 concluded that 'heredo-syphilitic tabes is more common than is generally supposed, but requires to be looked for, because it often manifests itself in an atypical form which does not attract attention.' He gives two examples in which the father was also tabetic: (1) A woman, aged twenty-two, had Hutchinson's teeth and signs of interstitial keratitis, and for the last two years presented the Argyll-Robertson pupil, lightning pains in the limbs, etc.; the father was tabetic, and had syphilis when the mother was pregnant, and infected her. (2) A girl of fifteen, the daughter of a tabetic father, showed the Argyll-Robertson pupil and syphilitic choroiditis. Similar cases have been reported by other observers.

Pseudo-tabes.—This term has been applied to cases closely simulating tabes, but differing in the presence of actual syphilitic changes in the posterior columns of the cord, instead of sclerosis, and also in being curable by specific treatment. This is a distinction without a difference, and is simply an additional proof of the syphilitic origin of tabes, showing also that tabes may be syphilitic in nature as well as in origin.

Heredo-syphilitic General Paralysis.—This may occur between the ages of eight and twenty, and is generally preceded by changes in character, loss of memory, etc. It is characterized by loss of muscular power, uncertain gait, spasmodic movements of the arms, tremors of the tongue, unequal pupils, and sometimes optic atrophy. It differs from the ordinary form of general paralysis in adults in the absence of the grandiose ideas, and appears to be more of the nature of a primary paralytic dementia. Two special characters are the arrest of physical development and sexual disorders. The average duration of the disease is four years, and it is equally common in both sexes.

In the case of juvenile general paralysis syphilitic heredity is the only essential cause, and alcoholism, sexual excess, overwork, etc., which complicate the etiology of the general paralysis of adults, are eliminated.

Raymond has reported a case of juvenile general paralysis in a girl of eleven years of age with signs of hereditary syphilis. At the autopsy the lesions of periencephalitis were found combined with the remains of former gummatous meningitis.

Parasyphilitic Epilepsy.—Epilepsy may probably be derived from parasyphilis, either in the acquired or hereditary disease. According to Fournier, syphilitic epilepsy proper is generally associated with other cerebral phenomena, advances more or less quickly towards a cure or fatal termination, and is often amenable to specific treatment. Parasyphilitic epilepsy, on the other hand, occurs as an isolated phenomenon, and continues so for a long time without the addition of other cerebral signs; also, it does not react to treatment. This leads us to the question of the syphilitic origin of so-called 'essential epilepsy.'

The Relation of Essential Epilepsy to Syphilis.—It appears that the only difference between syphilitic epilepsy and 'essential epilepsy' lies in the coexistence of other phenomena of cerebral syphilis, and that in the case of parasyphilitic epilepsy these are absent—at any rate, for a long time. What, then, is the difference between the so-called essential epilepsy and parasyphilitic epilepsy? In order to answer this question, it is necessary to examine other alleged causes of essential epilepsy.

Sir William Gowers states that 'an inherited tendency, indicated by the presence in ancestors or collateral relations of epilepsy itself, or of insanity, is traceable in rather more than a third of the cases. There is a family history of epilepsy in two-thirds of the inherited cases; of insanity in one-third; of both in one-tenth. Occasionally many members of a family suffer; in one instance no less than fourteen were epileptic, the cases being distributed through four generations. It is very doubtful whether any inherited morbid state, outside the nervous system, predisposes to epilepsy. A proclivity to phthisis has been thought to do so; but the evidence of statistics shows that this is an erroneous inference, due merely to the great frequency of consumption in the community. It

is doubtful whether any close relation exists between epilepsy and the inherited gouty diathesis, to which attention has been lately called. *Idiopathic epilepsy, however, sometimes occurs in the subjects of inherited syphilis, without other cause being traceable.* A strong predisposition to the disease often exists when there is defective general development of the brain from any influence acting on it in early life, or as a result of the congenital defect met with in neurotic families and in the offspring of consanguineous marriages. Three-quarters of the cases of epilepsy begin under twenty years, and nearly half (46 per cent.) between ten and twenty, the maximum being at fourteen, fifteen, and sixteen. One-eighth of all cases commence during the first three years of life.'

This evidence strongly supports the view of the heredo-syphilitic origin of so-called idiopathic epilepsy. Gowers admits (1) that idiopathic epilepsy sometimes occurs in the subjects of hereditary syphilis; (2) that it is predisposed to by defective development of the brain, which itself is known to be usually of syphilitic origin; (3) that it usually occurs under twenty years of age, the most common period for the manifestations of late heredo-syphilis; (4) that if there is not a family history of epilepsy there is frequently one of insanity, one of the chief causes of which is now known to be syphilis.

It would therefore appear that we are justified in concluding that so-called 'idiopathic' or essential epilepsy is a manifestation of hereditary syphilis. In this connection it is interesting to note that epilepsy and other nervous disorders have been shown to occur in the subjects of syphilis of the third generation (Chapter XX.).

Further evidence in support of the syphilitic origin of essential epilepsy is furnished by post-mortem changes in the brain. Turner has found that *endarteritis obliterans* and *defectively-developed nerve cells* are common in the brains of epileptics. He mentions the persistence of subcortical nerve cells which usually disappear in adult life. These are also present in imbeciles, who are often heredo-syphilitics.

It is not impossible that the whole subject of epilepsy (apart from traumatic lesions) may be regarded as belonging

to the domain of syphilis; and that 'idiopathic' epilepsy is a syphilitic or parasyphilitic phenomenon in the course of inherited syphilis, either of the second or third generations. On this assumption we may classify epilepsy into two classes, syphilitic and parasyphilitic.

1. SYPHILITIC EPILEPSY PROPER, or symptomatic epilepsy, may occur in acquired or hereditary syphilis, and is curable by specific treatment.

2. PARASYPHILITIC EPILEPSY, or the so-called 'essential' or 'idiopathic' epilepsy, is usually due to hereditary syphilis of the second or third generation, and does not react to anti-syphilitic treatment. It is also possible that some cases of parasyphilitic epilepsy are due to acquired syphilis.

The only important innovation in this classification is the substitution of the term 'parasyphilitic' for 'essential' or 'idiopathic.' The former term conveys a definite idea which is in accordance with facts; the latter terms are vague and meaningless.

Multiple Sclerosis.—Fournier suggested twenty years ago that multiple or disseminated sclerosis might be due to syphilis, for the following reasons: (1) Syphilis has a tendency to cause disseminated lesions in the cerebro-spinal axis; (2) it has a great tendency to cause sclerosis; (3) multiple sclerosis is recognised as an epiphenomenon in general infective diseases, and is due to arterial lesions.

Moncorvo, in 1883, reported several cases of multiple sclerosis occurring in young children affected with heredo-syphilis. He concluded that the disease was not uncommon in young subjects (from seven months to six years); that it presented the same symptomatology as the disease occurring in adults, and that hereditary syphilis must be included among its etiological factors. In two cases the disease was improved by antisyphilitic treatment. The following is a summary of one of Moncorvo's cases:

A girl aged seven years; born with evident signs of heredo-syphilis; convulsions during infancy; retarded development, both physical and mental; did not commence to talk till two years, or to walk till six years of age. General condition:

anæmic and puny; pigmental scars of former syphilides on body; natiform skull; swelling of the epiphyses; dental erosions. At the age of six, changes in character and irritability; strabismus and nystagmus; weakness of limbs with inco-ordination of movements; tremors on voluntary movement. Present state: weakness of lower limbs with staggering gait; weakness of upper limbs with inability to hold objects in one hand; tremors on voluntary movement; convergent strabismus; nystagmus, with horizontal and rotatory movements; dimness of vision; expression of imbecility; weak memory and change of character; scanning speech; tremors of tongue. Reflexes and sensation normal. All symptoms improved under six months' antisyphilitic treatment by mercurial inunctions and iodide of potassium.

Friedreich's Disease.—Dreyer Dufer has seen cases of hereditary syphilis simulate the signs of Friedreich's disease and yield to specific treatment. Combemale has also suggested the infectious origin of this disease. Moussons reported the case of a child of five years with tabo-cerebellar gait, absence of knee-jerks, symmetrical deformity of the feet, and signs of hereditary syphilis. He concluded that this was a case of heredo-nervous syphilis simulating Friedreich's disease, the lesions having undergone arrest under the influence of specific treatment. Ingelrans considers that there is a heredo-syphilitic form of Friedreich's disease, and has observed a typical case in a patient of twenty presenting stigmata of heredo-syphilis, whose father contracted syphilis a year before his birth. Oppenheim, however, regards these as false cases of Friedreich's disease, and attaches great importance to the sudden onset of symptoms, the periods of remission, affections of the optic nerve and the ocular muscles, intercurrent apoplectiform and epileptic attacks, etc.

Hermanides, in his work on Parasyphilis, includes neurasthenia and hysteria, progressive muscular atrophy, and spastic spinal paralysis among the parasyphilitic affections; and imbecility, idiocy, neurasthenia, hysteria, deaf-mutism, stammering, enuresis, and Raynaud's disease among the heredo-parasyphilitic affections. In addition to these there are the

dystrophic effects of heredo-syphilis which may be included in this category (Chapter XVII.).

The Possible Syphilitic Origin of Certain Types of Spinal Paralysis.

The differentiation of syphilis of the nervous system from the other classical types of paralysis is of great importance, especially as regards treatment. This does not, however, affect the question of the possibility of these classical types being of syphilitic or parasyphilitic origin. Tabes is probably not the only type of syphilitic origin.

Sir William Gowers gives the following etiological factors in the general pathology of diseases of the spinal cord:

1. *Neuropathic disposition*, or 'an inherited tendency to disease of the nerve elements, manifested by such affections as epilepsy and insanity.' The term 'neuropathic disposition,' in this connection, might be replaced by 'syphilitic heredity.' Moreover, epilepsy and insanity themselves are frequently of syphilitic origin.

2. '*Prolonged mental distress* sometimes sets up degenerative changes in some elements of the cord, especially in persons who are predisposed by neuropathic disposition.' This is included in No. 1, and requires no further comment.

3. *Injury*.—The immediate effects of injury by hæmorrhage, and the results of hæmatomyelia are obvious causes which do not concern us in this discussion. But the slow symptoms of impaired function, which come on some months after the injury, are possibly explained by a latent syphilis of the cord, which has been provoked by the injury acting as an accessory cause.

4. *Exposure to Cold*.—This is said to give rise to acute inflammation, chronic inflammation, or degenerative disease. It is difficult to accept this as a cause of paralysis except in cases which are predisposed by syphilitic heredity. Moreover, the members of the various Arctic and Antarctic expeditions do not appear to have suffered from any form of paralysis. Exposure to cold has been aptly termed 'the last refuge of destitute etiology.'

5. *Toxic agents*, such as lead and alcohol.

6. *Acute infectious processes*, such as septicæmia, cerebro-spinal meningitis, tetanus, and diphtheria, may act on the spinal cord, and gonorrhoea has been said to cause myelitis.

This group includes *syphilis*, concerning which Gowers remarks: 'Acute and chronic inflammations of the cord are often met with in syphilitic subjects, and have been thought to be, in many instances, of syphilitic origin. It is doubtful whether they present any syphilitic characters—*i.e.*, any histological features by which they differ from non-syphilitic inflammations. The evidence of dependence on syphilis is stronger in the case of chronic and subacute disseminated inflammation than in the case of acute myelitis. It may be, however, that inflammations due to other causes—*e.g.*, exposure—run a more acute course when they affect syphilitic subjects. The part thus played by syphilis in lessening the resisting power of the organism may be shared by other factors such as malnutrition and excesses of various kinds.'

From the examination of this evidence we most conclude that syphilis, at any rate, is the chief factor in spinal paralysis, either by the immediate or remote effects of the syphilitic microbe or its toxins, or by a predisposition caused by syphilitic heredity. Other causes, apart from injury and other acute infectious diseases, must be regarded only as accessory causes, and the chief of these is probably alcohol.

This being granted, it is better to assume that such diseases as multiple sclerosis, amyotrophic lateral sclerosis, progressive muscular atrophy, etc., are of syphilitic or parasyphilitic origin than to continue to regard them as due to vague and unknown causes.

This view is supported by the occurrence of transitional or intermediate forms between the different types of paralysis, and by the frequent existence of what are called atypical cases. Writing of primary spastic paraplegia (primary lateral sclerosis), Gowers makes the following suggestive remarks: 'Transitional forms are met with which constitute gradations between primary spastic paraplegia and other degenerations of the spinal cord. Slight inco-ordination may coexist in cases

approximating ataxic paraplegia. Cases may begin as pure tabes, and indications of lateral sclerosis may be superadded. Slight muscular wasting of the arms may be associated with indications of lateral sclerosis in the legs, and constitute a transition to the form of spinal muscular atrophy to which the name "amyotrophic lateral sclerosis" has been given. Very rarely considerable muscular wasting succeeds spasm in the same part. Spastic paraplegia also is often the early stage in cases which afterwards develop other symptoms characteristic of disseminated sclerosis. Nystagmus, however, may occur in cases otherwise offering no symptoms except those of lateral column affection. Unequivocal symptoms of syringomyelia have also been known to develop in a case which presented in its earlier stages the characteristic signs of primary lateral sclerosis.' Concerning the etiology of primary lateral sclerosis, Gowers states that 'the disease sometimes follows syphilis in a way to suggest a causal relation.'

It therefore appears that transitional forms are known to occur between certain types of spinal disease, which have been attributed to a syphilitic origin, such as primary lateral sclerosis, and others which have hitherto been regarded as not in any way connected with syphilis. As we have seen above, cases resembling Friedreich's disease have been found in the subjects of hereditary syphilis, and other cases have been found intermediate between Friedreich's disease and juvenile tabes. Yet the latter is regarded as of syphilitic origin and the former not so. Would it not be better to regard both as different types of the same heredo-syphilitic disease?

In syphilis we have infinite etiological possibilities. It is a disease which has a special predilection for the nervous system, any part of which it may affect directly by the gross lesions which it causes in the vascular system, and by the toxic effect of the syphilitic virus on the nerve cells; and indirectly by the degenerations which it may leave behind it in the neurones. It is therefore rational to regard syphilis as the chief factor in the causation of diseases of the nervous system, and more logical to attribute to it cases of paralysis of obscure etiology than to continue to include these among the number of diseases of unknown origin.

It may be true that typical syphilitic lesions may not be found post-mortem in these cases, but are syphilitic lesions always typical? The histological changes found in tabes are not typical of syphilis, yet tabes is of syphilitic origin. In fact, our ideas of what are to be considered as typical syphilitic lesions must be extended in order to include the whole of modern syphilology. This fact was drawn attention to by Professor Fournier at the recent discussion on general paralysis (p. 249).

The whole subject of parasyphilis, embracing lesions which are of syphilitic origin, but not of syphilitic nature in the usual sense of the term, has vastly increased the field of syphilis, and in no direction more than in diseases of the nervous system.

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CHAPTER XIII

THE EYE AND ITS APPENDAGES

Ocular syphilis is always grave, owing to the importance of the organ and to the multiplicity of lesions which may attack the cornea, retina, iris, and optic nerve. The smallest lesion may be followed by sclerosis, which will interfere with the function of the eye. Moreover, ocular syphilis is often a manifestation of syphilis of the brain; hence ocular syphilis means severe syphilis, and requires energetic treatment. The eye may be attacked by the primary, secondary, and tertiary lesions of the acquired disease; by parasyphilis; and by hereditary syphilis (Chapter XIX.).

Primary Chancre.

This is one of the forms of extragenital chancre (Chapter IV.), and usually affects the eyelid on its palpebral surface, causing eversion. It seldom occurs in the ocular conjunctiva. The chancre forms a hard, red, fleshy, indurated mass, eroded, but not ulcerated. The preauricular gland is enlarged. These characters differentiate it from any acute inflammatory affection of the eyelid, such as a stye, and from lupus and rodent ulcer.

The prognosis is usually good, but in neglected cases symblepharon, or adhesion of the ocular conjunctiva to the eyelid, may occur; also ectropion and entropion. Conjunctival chancre may favour the development of interstitial keratitis, and Treacher Collins has recently reported five cases of chancres which were complicated by keratitis from eighteen months to two years afterwards.

Secondary Lesions.

Keratitis.—This is described in the section on hereditary syphilis (Chapter XIX.). Although interstitial keratitis is *par excellence* an affection of the hereditary disease, it is said to occur occasionally in acquired syphilis (apart from the cases which sometimes follow chancre of the eye). According to Trousseau, keratitis in acquired syphilis is nearly always unilateral, of shorter duration, and less liable to relapse. There is less lachrymation and photophobia, and less vascularization of the cornea, which clears up more completely than in the keratitis of hereditary syphilis.

Scleritis and Episcleritis.—This consists in deep infiltration of the sclerotic with vascular subconjunctival projections. There may be concomitant iritis. According to Panas, the process consists in a gummatous infiltration of the uveal tract, commencing in the external surface of the ciliary body and extending to the sclerotic. The prognosis is bad, owing to the probable complications of the deep membranes, and also to the liability of the cicatrices to yield and cause bulging of the sclerotic.

Episcleritis consists in the development of small, hard nodosities under the conjunctiva near the cornea, of a violet colour, and traversed by episcleral vessels. They are generally associated with iritis.

Iritis.—This occurs in 3 or 4 per cent. of cases of acquired syphilis, generally about the sixth month. The symptoms consist in photophobia and lachrymation, diminution in vision, and neuralgic pains of varying degrees.

There is pericorneal injection of the anterior ciliary vessels; the iris is congested and thickened, and of a grayish colour; the anterior chamber is filled with plastic exudation, and the pupil is irregular, contracted, and reacts less readily to light. In mild cases the iritis subsides without leaving any trace, but in severe cases synechia, cyclitis, and disturbance of the vitreous may occur. Synechia of the iris to the lens causes disturbance of nutrition, and may eventually lead to opacity of the lens or atrophy of the globe. This form of *plastic iritis* is the usual form.

Serous Iritis is characterized by less corneal injection, and the rapid appearance of slight opacities in the anterior part of the vitreous. On the posterior surface of the cornea are seen small white spots, known as *keratitis punctata.* These are due to an affection of the aqueous humour, and the term keratitis is wrong. In serous iritis synechia is rare, but the intra-ocular tension is generally increased, so that atropine must be avoided, on account of the possibility of *glaucoma.*

Iritis is sometimes complicated by keratitis, which appears as an opaline patch of variable extent, which persists for some time and eventually causes a corneal opacity. A *papular* form of iritis may occur, characterized by the formation of small granules, of the size of a small pin's head, on the anterior surface of the iris near the pupil. Their colour varies from yellow to reddish-brown. These papules coincide with cutaneous syphilides, and are similar in nature.

Fournier states that congestive iritis sometimes occurs, without infiltration or gummata, as a late secondary phenomenon, and that such cases are mistaken for rheumatic iritis.

Gummatous Iritis.—True gummata of the iris are rare, nearly always single, and situated in the region of the ciliary body, in distinction to the papules which occupy the pupillary border. They may appear early in the secondary period or in the tertiary. The iris is swollen and of a yellowish colour, and the surface is covered with fine vessels. The gumma may attain the size of a small pea. After absorption it generally leaves atrophy of the tissue of the iris, and posterior synechia. It may open into the anterior chamber and cause hypopyon. Gummata of the iris are distinguished from tuberculous infiltration by their yellow or brown colour, while tubercles are usually white; also the latter are generally multiple, while gumma is almost always single.

Diagnosis.—Iritis is easily recognised by the above characters; the presence of pericorneal injection differentiates it from simple conjunctivitis. It is important not to confound iritis with an attack of *glaucoma.* The best means of diagnosis is by careful examination of the iris and pupil. The iris in iritis is thickened and congested with blood; the pupil generally

contracted and irregular; the tension somewhat diminished. In glaucoma, on the contrary, the iris is more or less shrunken, thin, and pressed forwards; the anterior chamber is shallow, and the pupil is generally a little dilated. The small black circle which limits the pupillary border internally, and is formed by the pigmented layer of the uvea, is hardly visible in the normal state, but becomes apparent in glaucoma. Lastly, the intra-ocular tension is increased.

But the diagnosis may be difficult in cases where the iritis is complicated by increased tension (*glaucomatous iritis*). There is then danger in the use of atropin, which, if used in glaucoma, may cause loss of the eye.

Prognosis.—This is always uncertain, as the affection is always serious. Relapses are not uncommon and recurrences frequent, especially when there are posterior synechiæ. These may cause complete occlusion of the pupil, and eventually glaucoma. Lastly, we must bear in mind that iritis is often the prelude to other ocular affections, and is sometimes complicated with choroido-retinitis. In cases of average severity with efficient treatment the prognosis is relatively benign, and the affection may be cured without leaving a trace. Moreover, of all the ocular manifestations of syphilis, iritis is the only one which may be said to have usually a good prognosis, the others being often the prelude to cerebral syphilis in process of evolution.

Treatment.—(*a*) If the tension of the eye is normal or diminished, a solution of sulphate of atropin (1 per cent.) should be instilled into the eye several times a day, according to the severity of the case. Atropin puts the iris at rest; it dilates the pupil and prevents contact of the iris with the lens, and so hinders the formation of adhesions (synechia), or ruptures those already formed, if not too resistant; it also relieves pain. Two or three leeches may also be applied to the temple to relieve congestion. Applications of warm compresses to the eye and the wearing of smoked glasses complete the local treatment.

(*b*) If the tension of the eye is increased, atropin must be avoided. Leeches to the temple and warm compresses should be applied, but atropin must be replaced by eserine. In

rebellious cases paracentesis of the cornea may be required to diminish intra-ocular tension. Iridectomy should only be performed in exceptional cases, for occlusion of the pupil or for glaucoma.

Cyclitis.—The ciliary body may be affected at the same time as the iris and choroid, constituting *irido-cyclitis*. Inflammation of the ciliary body is manifested by acute pain on pressure over the eyelids and diminished intra-ocular tension. Severe cases may end in destruction of the globe.

The lesion consists in cellular infiltration with vessels of new formation and disseminated foci of *endarteritis obliterans*. The choroid and retina often present foci of infiltration and small hæmorrhages.

Treatment in all cases is identical with that of iritis, by frequent instillations of atropin and warm applications to the eye. More or less numerous posterior synechiæ almost always occur, and sometimes there is total occlusion of the pupil.

Choroiditis. — The majority of cases of choroiditis are syphilitic, and all doubtful cases should be treated as such. The choroid is never affected by itself, the retina being always more or less implicated, and the different lesions should be grouped together as *choroido-retinitis*. The reason of this is that the retina only possesses vessels in its internal layers, the external layers, containing the rods and cones, being nourished by the choroid. Hence all lesions of the choroid interfere with their nutrition.

Disseminated Choroido-retinitis.—This is the most frequent form, and is characteristic of syphilis. It is often unilateral at first, and hence may not be noticed by the patient for some time. Objects are seen as through a mist, and there are gaps in the field of vision ; photopsia and hemeralopia also occur.

Examination with the ophthalmoscope shows a haziness of the papilla, which is due to the presence of numerous fine opacities in the posterior part of the vitreous. This condition persists for a variable time, with alternate periods of amelioration and aggravation, which are characteristic of the affection.

At the same time an eruption of nodules appears at the

periphery of the fundus oculi. Each one of these nodules consists of cellular infiltration of the choroid, and forms a yellow projection, surrounded by a pigmented circle. These develop continually all over the choroid, and often become confluent at certain points. Each one undergoes the same evolution; in a few weeks the nodule disappears, and the choroid in its place becomes atrophied, leaving a bluish-white spot, slightly excavated, formed by the denuded sclerotic and covered with small pigmented masses which may mask it completely. At the same time there is cicatricial contraction of the retina and destruction of the rods and cones. The papilla becomes decolourized, and finally atrophied.

This affection is essentially chronic, of long duration, and subject to recurrence. Finally optic atrophy occurs, usually with complete blindness, as the disease is nearly always bilateral. The nutrition of the lens is affected, and attacks of irido-cyclitis may supervene, which, when there is complete blindness, may necessitate enucleation, on account of the pain which they cause; but this is exceptional.

Irido-choroiditis.—We have already seen that in irido-cyclitis the choroid is often involved in the inflammation, and a true chronic choroiditis may exist at the same time as iritis, with affection of the vitreous and exudation in the anterior chamber.

Prognosis.—Whatever the variety observed, the prognosis is generally bad; it is nearly fatal in irido-choroiditis with much plastic exudation, and very serious in disseminated choroido-retinitis.

In the former papillary atrophy is the rule, and in the latter suppression of central vision. The prognosis is more favourable in anterior choroiditis, where the lesions are limited to the anterior segment, for this form is compatible with good vision.

Treatment.—General mercurial treatment should be intense, and administered by soluble injections. If these are begun early, before cicatricial changes have set in, excellent results may be obtained. After a first series of thirty injections and a few days' rest, a second or even third series may be repeated. At the same time as mercurial treatment sweating may be

promoted by means of infusion of jaborandi or injections of pilocarpin ($\frac{1}{6}$ grain two or three times a week). These injections are not dangerous provided they are made when the patient is confined to bed, but they should never be made away from home. Local treatment consists in the instillation of atropin drops, leeches to the temple, and warm compresses to the eye.

Retinitis.—Choroiditis is nearly always accompanied by changes in the retina (choroido-retinitis), but cases occur in which the lesion is chiefly confined to the retina.

In this case the changes are the same as in choroido-retinitis, with the absence of the eruption of nodosities. The functional troubles are also identical, consisting in progressive diminution of vision, photopsia, and colour-blindness, etc. The affection often remains unilateral. Like choroido-retinitis, the progress is essentially chronic, with alternate periods of amelioration and aggravation, and often ending in partial or complete blindness, in spite of treatment.

Syphilitic endarteritis is easily seen by ophthalmoscopic examination. The central reflection of the arterial wall, which exists normally, is only slightly apparent or even disappears, and on each side of the vessel is seen a white line, indicating sclerosis of the walls. Later on, when obliteration of the artery is complete, this is replaced by a thin white streak.

Endarteritis is always of grave prognosis, for it gives evidence of the state of the cerebral vessels, and cerebral lesions may occur a few months or years after endarteritis has been observed in the retina. Hæmorrhages and exudations may occur in the retina, and lead to the formation of gray streaks of cicatricial tissue.

Diabetic and albuminuric retinitis have been described as consequences of syphilis; also detachment of the retina consecutive to syphilitic choroiditis. Retinitis pigmentosa, which is nearly always of congenital origin, is dealt with in the chapter on hereditary syphilis of the eye (Chapter XIX.).

Optic Neuritis. — Syphilis of the optic nerve manifests itself by inflammatory or atrophic lesions, visible by the ophthalmoscope, or sometimes only by functional symptoms.

The subjective troubles are characterized by amblyopia, amaurosis, scintillating scotoma, and hemianopsia; but these are generally only slightly marked, and when they occur alone without objective signs they are of doubtful value in diagnosis. More commonly there are visible changes in the optic nerve and papilla.

The optic nerve, owing to its diverse relations during its course, may be affected by meningitis, arteritis, periostitis, orbital gumma, etc. But whatever the seat of the lesion, the papilla is nearly always affected, and shows visible changes resulting from compression or obstruction of circulation, caused by inflammation of the nerve trunk. Moreover, a lesion of the brain or meninges may react on the papilla, owing to the fact that the cerebro-spinal fluid circulates in the meningeal sheath of the optic nerve as far as the papilla. Lastly, the optic nerve is only separated from the sphenoidal sinus by a thin wall, which is sometimes perforated or even absent, and any inflammation of the sphenoidal sinus of the same side, or even of the opposite side, may set up optic neuritis.

Papillitis.—This is characterized by abnormal projection of the papilla, which overhangs the surrounding retina and becomes confounded with it. The limits have disappeared; the veins are large and tortuous, and small striated hæmorrhages occur around the papilla. The arteries, on the other hand, are very indistinct, and can often only be distinguished for a short distance from the papilla. At the same time their redness is exaggerated.

This appearance is due to obstruction of the circulation causing œdema. The inflammatory œdema causes diverse visual disorders. The field of vision is generally contracted, sometimes irregularly, and visual acuity is diminished to a variable extent.

This condition may be due to periostitis of the sphenoidal fissure, but in this case the affection is unilateral and accompanied by paralysis of the nerves of the orbit. Papillitis appears at a variable period, on the average about a year after the primary lesion, and is often complicated by iritis or irido-choroiditis.

Bilateral papillitis is one of the most constant signs of cerebral tumour or basal meningitis, and although there may be no symptoms of tumour and vision may be intact, neuro-papillitis is nearly always present. Papillitis is hence of great diagnostic importance.

Bilateral papillitis always presents the same characters, whatever the nature or seat of the tumour. It may be caused by any cerebral tumour or basal meningitis; in the case of syphilis, by gumma of the base or convexity, or by basal syphilitic meningitis. In this case prognosis is more favourable if early intense treatment is adopted. The papillary lesions may rapidly undergo resolution, and visual acuity may be restored. But more often when the papillitis has lasted a certain time the prognosis is less favourable. The papillary projection gradually disappears, loses its striated red aspect, and assumes a gray colour. The dilatation of the veins disappears, the arterial changes increase, and optic atrophy results, with total blindness.

Optic Atrophy.—There are two forms of optic atrophy, one following neuritis, and simple atrophy not preceded by inflammation of the papilla. The latter is called white or gray atrophy.

1. Post-neuritic Atrophy.—This is the usual termination of papillitis, which we have just dealt with. It differs from simple atrophy in several particulars: (1) The papilla does not recover its transparency, but assumes an opaque bluish-gray colour, and the vessels often become invisible. (2) The limits of the papilla are indistinct, and more or less confused with the retina. The border is irregular, and presents at certain points small pigmentary masses, the remains of former inflammation. (3) The veins are tortuous, the arteries narrow, showing the double white line indicating arteritis.

These characters, which are absent in simple atrophy, are diagnostic of gumma of the brain or basal meningitis.

2. Simple Atrophy.—The papilla loses its rose colour and becomes pale. The functional troubles consist in contraction of the field of vision, at first for colours, especially green. As the atrophy progresses the papilla becomes white, owing to

disappearance of the small vessels. The retinal vessels, on the other hand, are not affected, contrary to what occurs in post-neuritic atrophy. The edge of the papilla is clearly defined, on account of its white colour.

In some cases the papilla is bluish-gray, owing to changes in the nerve fibres. This is *gray atrophy*, and is especially found in tabes; *white atrophy* is generally due to a cerebral lesion. The distinction, however, is not always clearly marked, and in many tabetics the papilla is white.

Optic atrophy is the usual termination of choroido-retinitis and retinitis pigmentosa.

Treatment is only of any use in the earliest stage, and can have no effect when the atrophy is established.

Changes in the Optic Nerve.—Bony changes in the orbit and gumma at the base of the brain may affect the optic tract, and give rise to papillitis. Gummata of the optic nerve have been described. The symptoms caused are exophthalmos, motor paralysis, neuralgic pains from compression of the ciliary nerves, visual troubles, and change in the papilla.

The Lachrymal Apparatus.—Dacryoadenitis, forming a hard swelling in the upper and outer part of the orbit, is of rare occurrence, and is generally unilateral. It may coexist with iritis or other syphilitic manifestations of the eye. Affections of the lachrymal sac and ducts are generally the consequence of periostitis of the orbit.

The Orbit.—The chief syphilitic affection of the orbit is *osteoperiostitis*, which usually occurs at the orbital margin. The skin is raised and swollen, and painful on pressure. There is pain radiating to the temple, forehead, nose, and teeth; this is often intense, especially at night.

When periostitis affects the walls of the orbit there may be visual troubles from mechanical pressure. The eye is then displaced and its movements hindered, causing diplopia. If the cause is not removed, exophthalmos, optic neuritis, and optic atrophy may result. Periostitis may occupy the sphenoidal fissure, and affect all the nerves of the orbit. The inflammation may extend to the brain or to the Gasserian ganglion, causing *neuro-paralytic keratitis* (p. 281).

Orbital periostitis may generally be cured by treatment, but occasionally ends in suppuration, leaving a sinus leading to carious bone. This may result in cellulitis of the orbit and orbital pyæmia. This complication is said to be more common in tubercle than in syphilis.

Tertiary Lesions.

Tertiary lesions of the eye, as elsewhere, are more localized, but the visual troubles are often due to remote lesions, especially at the base of the brain. The eye, in fact, may be anatomically regarded as a prolongation of the brain, and is especially liable to be affected in cerebral syphilis. Excepting the cases of gummata limited to the envelopes of the eye and its annexes, all visual disorders appearing in the course of tertiary syphilis give evidence of a lesion situated at the base of the skull or brain, in the nuclei, or cerebral cortex, and are only epiphenomena in the course of cerebral syphilis.

It is hence difficult to follow a regular order in the description of these different lesions. A gumma of the base, for example, may determine visual disorders of different kinds according to its situation—neuralgia, paralysis of the ocular nerves, vascular changes, optic neuritis, etc. Inversely, the same visual disorder may be due to lesions of different nature, but situated in the same place.

For convenience of description the visual disorders of tertiary syphilis may be divided into three main groups, the first comprising gummata of the globe of the eye and its annexes, the second motor troubles, and the third sensory disorders, including neuralgia and paralysis of the trigeminal.

1. Gummata of the Globe and its Annexes.

Gummata of the cornea and sclerotic have been described, but are rare. Gummata may occur in the iris, ciliary body, or choroid. *Gummatous iritis* has been already mentioned. The iris is rarely affected alone, and when this occurs the diagnosis from tubercle is very difficult. In such cases it may be deter-

mined by inoculation of the guinea-pig with aqueous humour, as a test for tubercle.

The *ciliary body* is the seat of predilection for gummata of the uveal tract, and they have been described as occurring two or three months after the chancre. The process begins with a plastic iritis, followed by a dark red swelling near the corneal margin. This projection becomes yellow, and is transformed later into a fungoid growth which may resemble tubercle. The iris is always affected by extension, and the anterior chamber contains a fibrinous or even purulent deposit, due to softening of the gumma. The iris is discolored and atrophied, and forms posterior synechiæ. The sclerotic may be rapidly perforated, and in severe cases there may be atrophy of the globe. Gummata of the ciliary body may coexist with gummata elsewhere.

Diagnosis from tubercle is sometimes difficult, and may depend on other signs of syphilis. Prognosis is always bad, owing to the tendency to destruction of the globe. Sometimes cases are cured, with complete restoration of function; but this is not the rule, and there is generally considerable affection of vision, and sometimes atrophy of the globe.

Treatment by mercurial injections should be intense, and atropin applied to the eye frequently. The intra-ocular tension must be carefully watched, and mydriatics suspended if there is any increase in tension. Later on iridectomy may become necessary.

The *choroid* is less often attacked by gumma than other parts of the uveal tract, apart from the small nodosities occurring in choroiditis. Gumma of the choroid arises as a white prejection in some part of the fundus, which is rapidly complicated by iritis, optic neuritis, and often bulging of the sclerotic. It may be mistaken for sarcoma, but the favourable influence of treatment clears up the diagnosis. In all cases atrophy of the choroid and retina takes place in the region of the gumma.

Gumma of the *eyelid* is less common than chancre. It is connected with the tarsal cartilage, and may simulate a chalazion. Sometimes it infiltrates the whole thickness of the

eyelid, constituting syphilitic tarsitis. It generally ulcerates, but is distinguished from epithelioma by the tendency to cicatrization.

2. Motor Affections.

Ocular Paralysis.—Syphilis is the principal cause of paralysis of the muscles of the eye. Ocular paralysis usually belongs to the later phenomena, but has been observed within the first few months. It also occurs in tabes and general paralysis.

The frequency of paralyses of the eye muscles is due to the multiplicity of the lesions which may cause them: gummata of nerves, meninges, or bone; gummatous periostitis, compressing the nerves at the base of the skull; arteritis, causing foci of hæmorrhage and softening; and sometimes gumma of the globe.

The *signs of paralysis* consist in deviation of the eye to the opposite side of the paralysis, diplopia, and sometimes headache, vertigo, and nausea.

Diplopia is the chief sign, and by itself confirms the existence of paralysis. The only possible error is to mistake paralysis for a strabismus; but in the latter there is no diplopia, and the course of the affection is different. Strabismus occurs in childhood, and is not accompanied by diminution in the mobility of the eyes. Whatever the situation of the fixed object, the eyes converge towards it, the one fixing it and the other missing it. On the contrary, in paralysis of an ocular muscle there is diplopia with diminution or absence of mobility in the paralyzed side, while in all other directions the position of the two eyes is normal.

The character of the diplopia shows which muscles are paralyzed. Diplopia is said to be *homonymous* when the false image is on the same side as the paralysis, and *crossed* when the image seen by the paralyzed eye appears on the sound side. All homonymous diplopia results from the paralysis of an abductor muscle, all crossed diplopia from paralysis of an adductor. The image is always deviated to the side of the paralyzed muscle.

Paralysis of the Third Nerve.—This is the most common paralysis, and may be complete or partial. In complete paralysis there is ptosis, immobility of the globe, which is deviated outwards by the external rectus, and dilatation of the pupil. Partial paralysis gives rise to different symptoms according to the branch of the nerve which is affected. Paralysis of the sphincter and ciliary muscle constitutes *ophthalmoplegia interna*. This is generally unilateral, and may be caused by different diseases; but 75 per cent. of the cases are caused by syphilis. In this condition there is paralysis of the pupil and paralysis of accommodation. It is generally incurable, and often constitutes the first stage of general paralysis.

Paralysis of the Sixth Nerve.—This is more uncommon, and causes deviation of the eye inwards and homonymous diplopia. The seat of the lesion is generally peripheral, and may be caused by gumma in the orbit, or sphenoidal fissure, or at the base of the skull. The lesion may be intrabulbar, and is then accompanied by facial paralysis on the same side and hemiplegia on the opposite side.

Attacks of Jacksonian epilepsy may occur at the same time as paralysis of the external rectus. This indicates gummatous meningitis in the region of the motor centres.

The prognosis of paralysis of the sixth nerve is not unfavourable, because the nucleus is rarely affected, and when the paralysis has not lasted too long it may be cured.

Paralysis of the Fourth Nerve.—The fourth nerve, or *patheticus*, is rarely affected. When it occurs, paralysis of the superior oblique muscle results in homonymous diplopia, with the false image obliquely deviated downwards and outwards. It generally coexists with paralysis of the third and other nerves.

Diagnosis of the Seat of the Lesion.—The lesion may be situated in the orbit, the sphenoidal fissure, the base of the skull, the nuclei of the nerves, or the cerebral cortex. The syndrome is very variable according to the seat of the paralysis, and is sometimes associated with paralysis of other cranial nerves, such as the trigeminal, or even with hemiplegia and aphasia.

1. Periostitis of the Orbit. — Gummatous periostitis generally occurs at the upper margin of the orbit as a painful swelling, causing pseudo-ptosis by infiltration of the eyelid. There is concomitant exophthalmos, and other nerve branches may be affected in proportion to the gummatous proliferation in the depth of the orbit. The three motor nerves of the eye may be affected, causing partial or total ophthalmoplegia. Total paralysis of the third nerve, without implication of the fourth and sixth, suggests an orbital affection.

2. Periostitis of the Sphenoidal Fissure.—Owing to the anatomical character of this region, there is nearly always total ophthalmoplegia with ptosis. The three motor nerves are affected in their passage through the fissure, and there is complete immobility of the eye. There is also complete insensibility of the cornea, the conjunctiva, and all the cutaneous region supplied by the first branch of the trigeminal nerve.

Vision is often diminished by extension of inflammation to the optic foramen, causing papillitis of varying degrees. Sometimes there is deep orbital pain, swelling of the upper eyelid, and slight exophthalmos.

This group of symptoms—paralysis of the third, fourth, and sixth nerves, and the first branch of the fifth, while the whole region supplied by the inferior maxillary nerve is unaffected—is characteristic of a lesion of the sphenoidal fissure. In lesions at the base of the skull all branches of the fifth—or at least, the two first branches—are affected, and the paralysis of the motor nerves of the eye is generally accompanied by paralysis of the facial, the auditory, or the hypoglossal. When the lesion is intra-orbital it is rare for all the three motor nerves to be simultaneously affected.

Prognosis is relatively good if treatment is instituted in time, and the symptoms may disappear without leaving any trace.

3. Basal Lesions.—The most common basal lesion is gummatous meningitis, which is usually situated in the region of the chiasma and crura cerebri, where the two motor oculi nerves have their apparent seat of origin, and are contiguous in the interpeduncular space. The nerves become included in

a glutinous mass formed of vascular granular tissue, enclosing thrombosed and obliterated vessels.

The symptoms consist in headache, vomiting, vertigo, loss of consciousness, diminished intelligence, and loss of memory, and paralysis of one or more cranial nerves. On account of the predilection of the lesion for the interpeduncular space, the third nerve is the most frequently attacked. The paralysis is total and often bilateral, owing to the proximity of the nerves at their origin.

Sometimes there are gummatous tumours, or exostoses, which compress the nerves; or arteritis of the posterior cerebral and superior cerebellar arteries, which are in close relation with the third nerves. Lastly, there may be gummatous infiltration of the nerves themselves.

4. Lesions of the Nuclei of the Oculomotor Nerve.—These are nearly always due to vascular changes in the basilar artery, which gives small branches through the posterior perforated space to supply the nuclei of the third nerve. These are all terminal arteries, and hence a lesion in the basilar artery or one of these branches causes total or partial paralysis of the third nerve. Partial paralysis is more frequent, especially paralysis of the levator palpebræ and ophthalmoplegia interna.

The prognosis is generally bad. Sometimes the vessels are free, and there is a gummatous infiltration extending to the nuclei, and destroying them totally or partially. The roots of the nerves may be involved in the growth, and the cerebral peduncle more or less destroyed. Lastly, primary degeneration of the nuclei has been noted, as is seen in tabes. In all these cases the symptoms vary with the extent of the lesion, and the paralysis may be total or partial.

5. Cortical Lesions.—The seat of predilection of cerebral syphilis is gummatous meningitis of the base, but cortical lesions may also occur, giving rise to paralyses which are nearly always partial, and often associated. The most common ocular lesion is ptosis. The path followed by the optic tracts from the nuclei to the cortex is not known, but an intracerebral gumma may attack them in any part of their course.

Sensory Affections.

Neuralgia and Paralysis of the Trigeminal.—Neuralgia of the fifth nerve may arise early in the course of syphilis, or in the tertiary period. It may be total or localized to one or two branches of the nerve. In tertiary syphilis it is observed under two different conditions: (1) Osteoperiostitis or gummata compressing the nerve in the orbit, or in the region of the Gasserian ganglion; gummata of the retro-ocular tissue, and periostitis of the superior maxilla affecting the ophthalmic and superior maxillary branches of the fifth nerve; tertiary rhinitis with destruction of the septum. (2) In the second place, the neuralgia is met with as a parasyphilitic manifestation. Tabetic neuralgia of the trigeminal affects only the sensory branch, leaving the masticatory branch intact.

With the progress of the lesion absolute loss of sensation may appear in all the regions supplied by the fifth pair, accompanied or not with neuroparalytic keratitis. Sometimes there is a true painful anæsthesia, the neuralgia coexisting with cutaneous anæsthesia. The pain is not usually continuous, but occurs in paroxysms, which sometimes coincide with transient paralysis of the oculomotor. This painful anæsthesia may be explained by interruption of the centrifugal conduction at the level of the lesion; but the irritation of the nerve resulting from the lesion is still transmitted as far as the nuclei of the fifth pair, whence the pain is felt.

Neuroparalytic Keratitis.—This is one of the most frequent and formidable complications of affection of the trigeminal. It consists in insensibility of the cornea, often ending in perforation. It may be caused by a lesion affecting any point of the nerve or its nucleus, or the Gasserian ganglion.

It is sometimes preceded by intense periorbital pain. The corneal lesion generally appears suddenly, without appreciable cause, and without any premonitory symptoms. In the first stage there is diffuse opaline infiltration of the cornea, with absolute insensibility. There is no conjunctival reaction, pericorneal injection, or photophobia. The ulceration appears

generally at the lower part of the cornea, and rapidly causes perforation, with more or less prolapse of the iris and all its consequences. Sometimes the process is so rapid that perforation may occur the day after infiltration, especially in children. At other times the termination is relatively favourable, the infiltration does not end in perforation, and the opacity may be partly repaired.

The affection is nearly always unilateral, but may be bilateral in cases where the lesion is situated in the region of the chiasma or the interpeduncular space.

Associated Symptoms.—(1) There may be anæsthesia of the skin and mucous membrane of the same side in the whole region supplied by the trigeminal. (2) Sometimes paroxysmal headache precedes the keratitis. (3) Paralysis of the third, sixth, and seventh nerves may occur, and even auditory affection of the same side; or optic atrophy if the lesion is situated in the large branches of origin of the trigeminal. (4) There may be paralysis of the sympathetic, with contracted pupil, diminution in the palpebral fissure, and sinking of the globe. (5) Finally, there may be aphasia with right hemiplegia, associated with left keratitis.

Diagnosis.—The absence of reactional phenomena and the absolute insensibility of the cornea distinguish this affection from interstitial keratitis. Keratomalacia is nearly always bilateral and only seen in infancy, and is characterized by fatty transformation of the epithelial cells on the surface of the cornea.

Syphilis is recognised by all as a cause of the affection, but other causes may be injury to the nerve trunk or the Gasserian ganglion by fracture of the base, gunshot wound, tumour, or hæmorrhage, or tubercle in the nuclei of the nerve, etc. Diagnosis must be based on the coexistence of other symptoms and on the influence of treatment.

There are various theories as to the pathogeny of the affection. Removal of the Gasserian ganglion appears to show that the trigeminal does not contain direct trophic fibres, as the classical experiments of Magendie seemed to show. The two chief theories of the origin of the keratitis are the trau-

matic and microbic. According to the former, keratitis is caused by the irritation of the cornea by foreign bodies which are not washed away by the tears, owing to the insensibility of the cornea. This, however, will not apply to most cases. The second theory assumes that the cornea is rendered liable to microbic invasion by its diminished nutrition. Each hypothesis is partly true, but incomplete.

It must be borne in mind that a lesion of the fifth nerve is the basis of all neuroparalytic keratitis, but does not cause it necessarily. This only occurs in about half the cases. The ciliary ganglion may possibly be the cause of the affection, and it has recently been shown that removal of this ganglion in the cat caused neuroparalytic keratitis in three cases out of five.

The treatment consists in intense mercurial treatment and antiseptic applications locally. The prognosis is bad, but better in syphilitic cases than those due to other causes.

General Treatment of Ocular Syphilis.

Ocular syphilis always requires energetic mercurial treatment. For this purpose either inunctions or injections may be used. Terrien prefers injections of biniodide of mercury in a series of twenty-five to thirty daily injections, or gray oil in a series of four or five weekly injections. In desperate cases, or when the above methods fail, he resorts to calomel injections.

Jullien has reported a case of optic neuritis which was cured by injections of calomel (5 centigrammes every five or six days) after cyanide and biniodide injections had failed. In this case the other eye had been enucleated for supposed sarcoma a few months previously.

Subconjunctival injections have been recommended by certain surgeons in cases of choroiditis, retinitis, irido-cyclitis, sclerotitis, and keratitis; but, according to Terrien, their therapeutic value has been exaggerated. Two or three drops of sublimate or cyanide (1 in 1,000) are injected into the subconjunctival tissue every four or five days, by pinching up the conjunctiva

and inserting the needle parallel to the sclerotic. Cocaine is applied to the eye first.

Iodide has little influence in cases of choroido-retinitis or optic neuritis, and should be reserved for gummatous lesions, in association with mercury.

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CHAPTER XIV

GENERAL TREATMENT OF SYPHILIS

In the present state of our knowledge there are only two drugs which possess any antisyphilitic action—viz., mercury and iodides. Whether these drugs will ever be replaced by some form of serum-therapy is problematical, and at present all attempts at serum treatment have proved unsatisfactory. Of the two antisyphilitic remedies, mercury is by far the more important. Iodides must be regarded as of secondary importance, although of great value in the later stages of syphilis.

Abortive Treatment.—Many attempts have been made to abort syphilis by destruction or excision of the chancre, but none of these attempts have been definitely successful. The chancre has been excised a few hours after its appearance; the lymphatic glands have been removed; an abrasion has even been excised before any chancre appeared; but all these measures have failed to prevent the development of constitutional syphilis. The failure of these abortive methods is due to the fact that syphilitic infection of the system takes place very rapidly, both by the lymphatics and bloodvessels. When the chancre appears the organism is already entirely infected, or, at any rate, the infection has extended over an area too large for any form of excision to cope with.

The recent experiments of Metchnikoff, however, seem to show that syphilitic infection may be prevented by early inunction of the point of inoculation with 30 per cent. calomel ointment. After establishing this fact by a series of experiments on monkeys, the experiment was tried on a medical student who volunteered for the purpose. Syphilitic virus from two chancres was inoculated by scarifications in the

balano-preputial furrow. At the same time four macacus monkeys were inoculated with the same virus. An hour after inoculation calomel ointment was rubbed into the scarifications for eight minutes in the student and in one of the monkeys. Twenty hours afterwards the same treatment was applied to another monkey. The two remaining monkeys were kept for control, and developed syphilitic chancres seventeen days after inoculation. The monkey treated twenty hours after inoculation developed a chancre on the thirty-second day. No sign of syphilis appeared in the student, nor in the monkey treated at the same time, up to three months after the experiment.

Although these experiments may require further confirmation, they tend to show that syphilis may be prevented by mercurial inunction of the point of inoculation an hour after infection. The practical application of this discovery is limited, owing to the fact that the point of inoculation is not known with certainty unless there is an abrasion. Moreover, patients seldom apply for treatment within an hour of possible infection. However, if such a case presents itself, inunction with calomel ointment of the supposed point of inoculation is indicated.

Mercury.

All authorities agree that mercury is the chief remedy in the therapeutics of syphilis, but opinions differ as to the mode of administration, the preparations to be used, and the duration of treatment. These questions will be dealt with shortly.

Action of Mercury.—There is a general idea that mercury acts by its bactericidal action on the syphilitic microbe, and that the therapeutics of syphilis consist in graduating the dose of the drug so as to combat the syphilitic virus without causing damage to the patient from the poisonous effect of mercury.

It is also possible that mercury acts indirectly by causing the production of *alexins*—*i.e.*, substances furnishing the organism with the power of defence by neutralizing the pathogenic agent. The organism certainly plays an important part in the cure, and appears to furnish a special antitoxin. This action is shown by cases of syphilis which undergo

spontaneous resolution without treatment. But it is probable that mercury has also a direct specific action, considering its frequently rapid effects, which are difficult to explain otherwise.

According to some observers mercury circulates in the serum as a chloro-albuminate; according to others in the white corpuscles as reduced mercury in a state of fine division. The leucocytes may therefore have a double action by absorbing the microbes and carrying mercury, and a diminution in leucocytes in the course of treatment is an unfavourable sign.

Mercury is partly excreted by the urine, and partly retained in the tissues, to be slowly eliminated later on. After an injection of calomel, mercury appears in the urine in a few hours, and retains its maximum on the fifth day. With inunction and ingestion excretion is slower, and does not take place till the fifteenth to twenty-fifth days. Hence injections are more rapid. If the portion of mercury retained by the tissues accumulates beyond the point of toleration toxic effects are produced, owing to insufficient elimination. Mercury, when circulating in solution, has less action than when deposited in the tissues, because it is eliminated more quickly by the urine. Hence it would appear that the best preparation of mercury to use is metallic mercury itself, which is eliminated more gradually. This is in favour of treatment by blue pill internally, and by gray oil hypodermically.

Mercury has a remarkable action on syphilitic neoplasms, and generally causes them to disappear in the course of a few weeks' treatment. It is especially indicated in the primary and secondary stages of syphilis, but should also be continued in the tertiary stage in combination with iodides. Mercurial treatment has both a *curative* action on present lesions and a *preventive* action on future manifestations. The administration of mercury during the primary stage attenuates the secondary symptoms to a considerable extent, and in some cases may render them inappreciable. It is also proved that prolonged mercurial treatment during the early stages of syphilis is the chief safeguard against the development of tertiary syphilis.

Toxic Effects of Mercury.—Mercurial intoxication is manifested by the following effects: (1) Stomatitis; (2) gastro-

enteritis; (3) cutaneous eruptions; (4) general disorders of nutrition. These effects may follow the administration of mercury by any method, whether by ingestion, inunction, injection, or fumigation.

STOMATITIS.—In former times, when salivation was regarded as essential in mercurial treatment, severe forms of mercurial stomatitis were common, with profuse salivation, ulceration of the gums, loss of teeth, and even necrosis of the jaws. Nowadays such cases are seldom seen, and the appearance of stomatitis is regarded as a sign to suspend treatment. Some patients have a peculiar idiosyncrasy for mercury, and cannot take it even in small doses without suffering from stomatitis; but in most cases stomatitis may be prevented during a course of mercurial treatment by careful attention to the hygiene of the mouth. The mouth should be rinsed after each meal with a lotion containing chlorate of potash and alum, and the teeth should be brushed twice a day with a dentifrice containing powdered charcoal, chlorate of potash, etc. (see Appendix for formulæ).

The *symptoms* of mercurial stomatitis consist in redness and swelling of the edges of the gums, salivation, a peculiar fœtor of the breath, swelling of the tongue, and, later on, ulceration and bleeding of the gums. The stomatitis is usually localized at first, either to the gum and mucous membrane of the cheek adjacent to the last molar tooth, or to the lower incisors.

Patients should always be warned of the possible occurrence of stomatitis when taking mercury, and should be told to discontinue it on the first sign of soreness of the gums.

The *treatment* of mercurial stomatitis consists in suspension of mercurial treatment for a time, and the substitution of a mixture containing 10 grains each of chlorate of potash and iodide of potassium to the ounce, three or four times a day. The mouth should be frequently rinsed with the chlorate of potash and alum solution, or with oxygenated water. If there are ulcers of the gums or tongue, these may be painted with dilute tincture of iodine (1 in 10).

GASTRO-ENTERITIS. — In some cases mercury causes dyspepsia, and occasionally colic and diarrhœa. In exceptional

cases ulcerative colitis has been said to occur. The gastric and intestinal complications of mercury appear to vary with the nature of the mercurial preparation, and are more common with the perchloride than with other mercurial preparations.

Cutaneous Eruptions.—Eruptions caused by the absorption of mercury are rare, and are generally due to some idiosyncrasy of the patient. The most common type is a *desquamative erythema*, which may be easily mistaken for erythema multiforme, erysipelas, etc. In other cases the eruption is urticarial, morbilliform, scarlatiniform, or eczematous. Several of these types of eruption may occur at the same time on various parts of the body. Desquamation may be branny, or in large flakes as in scarlatina. There is generally some pruritus, and febrile symptoms may occur.

Nutritional Disorders.—Mercury, when given in large doses or for too long a period, may cause a condition of anæmia with emaciation, and disturbance of nutrition may also be caused by mercurial enteritis and dyspepsia; but these effects seldom occur with the ordinary medicinal doses.

Effect of Mercury on the Kidneys. — As mercury is actively eliminated by the kidneys, it is natural to suppose that these organs may sometimes suffer from the action of the drug, and cases of albuminuria and hæmaturia have been reported by many observers. It is more than probable, however, that most cases of so-called *mercurial nephritis* after moderate doses of mercury which have been reported are really cases of early syphilitic nephritis.

In any case it is advisable to examine the urine for albumin before commencing a course of mercury, and if there are signs of insufficient renal permeability mercury should be given cautiously and in small doses; otherwise there is a risk of mercurial intoxication from deficient elimination by the kidneys. But if the albuminuria appears to be of syphilitic origin, it will usually yield to mercurial treatment (p. 187).

Methods of Mercurial Treatment.

There are four methods of administering mercury—(1) ingestion by the mouth; (2) inunction through the skin; (3) subcutaneous injection; (4) fumigation.

Ingestion is the simplest method, and in many cases the only one which is practicable. It is sufficient for the majority of cases of syphilis, and is the most convenient method for prolonged treatment; but when severe symptoms arise, for which rapid mercurialization is required, recourse should be had to inunction or injection. It is also wise to commence a course of mercurial treatment with one of these methods till the first outbreak of symptoms has subsided, after which treatment can be continued by ingestion.

Ingestion.—Mercury may be given by the mouth in the form of a mixture or as a pill, the latter being by far the more convenient method. The chief mercurial preparations used for this purpose are the ordinary blue pill, hydrargyrum cum creta, the proto-iodide of mercury (green iodide), the perchloride (in the form of Dupuytren's pills), the tannate, and calomel in the form of Plummer's pill. The pill most generally used in France is a modification of Ricord's proto-iodide pill; those most in vogue in England are blue pill and hydrargyrum cum creta.

Fournier recommends *proto-iodide* pills, 5 centigrammes twice daily, especially during the early stages of syphilis. In men the daily dose should be 10 centigrammes; in women 7 or 8 centigrammes. Proto-iodide, however, is more liable than other preparations to cause stomatitis. *Perchloride of mercury*, in the form of Dupuytren's pills, is liable to cause gastric and intestinal complications, and has less action on early syphilitic lesions than the proto-iodide. For these reasons it appears better to use metallic mercury as a routine method, either in the form of *blue pill* (2 grains two or three times a day) or *gray powder* (1 or 2 grains three or four times a day), according to symptoms. To prevent diarrhœa the blue pills should be combined with $\frac{1}{6}$ grain of opium and the gray powder with 1 grain of compound ipecacuanha powder.

The *tannate of mercury* has been advocated because it is said not to be absorbed till it reaches the intestine, and thereby avoids irritation of the stomach. But the tannate is an unstable preparation, and has less therapeutic action than other preparations. The *salicylate of mercury* is also used by some in the form of pills containing $\frac{1}{4}$ or $\frac{1}{6}$ grain of the salt.

Perchloride of mercury and *biniodide* may be given in solution, and the latter is useful in the later stages of secondary syphilis. If the B.P. liquor hydrarg. perchlor. is used, the dose should be 2 drachms.

Inunction.—This is the oldest method of mercurial treatment, and is still one of the most useful when rapid mercurialization is required. By this method mercurial ointment is rubbed into the skin for fifteen or twenty minutes; the mercury penetrates the cutaneous glands, and from these is absorbed into the blood. It has been said by some authorities that mercury administered in this way is not absorbed by the skin, but by the lungs in the form of vapour. This statement has been disproved by the fact that mercury has been shown to penetrate the skin by post-mortem examination of patients who have recently undergone inunction, and also by experiments on animals. Although a certain amount of mercury when spread on the skin becomes volatilized, this amount will not account for the rapid effect produced by mercurial inunction.

Technique.—The best ointment to use for inunction is the *unguentum cinereum*, composed of equal parts of mercury and lanoline, with a sufficiency of olive oil. About a drachm of this is rubbed into the skin daily for fifteen to twenty minutes, varying the site of inunction on each occasion. Parts of the body where the skin is thin and free from hairs should be chosen—the inner side of the thighs and arms and the sides of the thorax being treated in turn, so that a different part of the body is treated every day. The rubbing is best done at night, after which the patient should go to bed in a flannel night-shirt In the morning a warm bath should be taken, and the remains of the ointment washed off. At Aix-la-Chapelle the rubbing is performed by a professional rubber, and the treatment is

combined with sulphur baths and the drinking of sulphur waters. The patient can perform the operation himself if there is no necessity for dissimulation. In cases where it is wished to keep the treatment secret, application of the ointment to the soles of the feet has been recommended, but this method is incomplete and unsatisfactory.

Advantages and Disadvantages.—The advantages of mercurial inunction are — (1) rapid therapeutic action; (2) avoidance of the digestive tract, which is left free for the administration of other remedies, such as iodide of potassium, tonics, etc. The disadvantages are—(1) the inconvenience and dirt; (2) the revelatory nature of the treatment from staining of the linen. One of the chief advantages of undergoing a course of treatment at Aix-la-Chapelle is the possibility of keeping the treatment secret and avoiding scandal. Many patients visit these Continental watering-places for 'rheumatism' (syphilitic or otherwise), and can undergo their treatment without advertising the fact that they are suffering from syphilis.

The duration of the inunction treatment, the number of rubbings, and the amount of ointment to be used, vary according to the severity of the disease and the tolerance of the patient to mercury. In an average case two courses of three weeks' daily inunction may be given, separated by a week's interval. The treatment must be guided by careful attention to the state of the mouth, and the rubbings should be suspended if stomatitis occurs. The liability to sudden general stomatitis is one of the few objections to the method.

Subcutaneous Injection.—This method, introduced by Scarenzio in 1864, is the most recent addition to the therapeutics of syphilis. Mercury may be administered by *soluble injections* every day or every other day, or by *insoluble injections* performed once a week. Most authorities prefer intramuscular injections, but Lang, Gaucher, and others inject into the subcutaneous tissue only. Lang, who always uses gray oil injections, injects into the subcutaneous tissue of the back.

According to Balzer, an injection of mercury is distributed as follows: (1) A part is absorbed at once and transformed in

the blood or tissues; (2) a residual part remains at the focus of injection, combined with the serum in the form of albuminate, and is absorbed slowly later on; (3) a part is fixed in the organism, in the liver, kidneys, intestine, and other viscera; (4) a part is eliminated daily in the urine, and this varies very little whatever the dose injected, or whatever the method of mercurialization employed. The accumulation of fixed mercury in the organism thus gradually increases proportionately to the doses injected. It is therefore logical to inject only that amount of mercury which can be eliminated in twenty-four hours, which may be called the physiological dose; but this dose must often be exceeded in order to produce more rapid therapeutic effects. However, the dose should not be greater than the organism can utilize, for certain lesions only yield to prolonged treatment, which must be carried out with small doses. The average *daily dose of mercury* required by the organism is said to be 1 *centigramme* (about $\frac{1}{6}$ grain).

Technique of Intramuscular Injections.—(1) The site usually chosen is the *posterior third* of the buttock, so as to avoid the sciatic nerve and vessels. (2) The injections are made deeply into the muscle, using each buttock alternately. (3) The syringe should be of glass, so as to be easily sterilizable, and the needle should be of platinum-iridium, and about 1½ inches long. (4) The skin should be washed with soap and water, and afterwards with carbolic lotion, and the needle should be sterilized by passing through the flame before each injection. (5) After insertion of the needle, the piston of the syringe should be slightly withdrawn, and if any blood appears the needle should be reinserted, so as to avoid injection into a bloodvessel.

The chief of the *insoluble* preparations used for injection are gray oil, calomel, salicylate, and thymol acetate; the chief of the *soluble* preparations are biniodide, perchloride, sal alembroth, benzoate, cyanide, succinimide, cacodylate, sozoiodolate, and hermophenyl.

Gray Oil Injections.—Injections of gray oil are still used for the routine treatment of syphilis by Lang of Vienna, who introduced the method, and have been extensively employed

by Lambkin in the treatment of syphilis in the British army. Lambkin's formula is as follows:

Mercury	...	...	...	1 ounce (by weight)
Anhydrous lanoline	...	...	...	4 ounces ,,
Liquid paraffin (carbolized to 2 per cent.)			to 10	,, (by volume)

This contains 1 grain of mercury in 10 minims, and 15 minims (1½ grains of mercury) is a full dose. It is difficult to suspend more than a grain of metallic mercury in 10 minims of an oily vehicle. Lambkin gives the following directions for the preparation of his 'mercurial cream,' which is essentially the same as Lang's gray oil: The mercury and lanoline are rubbed together in small quantities in a glass mortar till the particles of mercury become invisible. This process of trituration takes about two hours, but is essential. After this the carbolized liquid paraffin is added. The cream is kept in wide-mouthed glass-stoppered bottles, and before use should be well stirred up with a glass rod dipped in boiling olive oil. In cold weather the cream becomes semi-solid, and requires warming in a water-bath; in the tropics, on the other hand, it requires to be placed in an ice-chest, as the mercury is liable to sink to the bottom of the vessel. Injections are made on an average once a week with doses of 10 to 15 minims (containing 1 to 1½ grains of mercury), but the dose and frequency of injection must vary according to the nature of the case.

Gray oil injections constitute one of the best methods for the routine treatment of syphilis in its earlier stages.

Calomel Injections. — Injection of calomel is probably the most powerful method of administering mercury. Calomel injections are, therefore, not suitable for the routine treatment of syphilis, but should be reserved for urgent cases where a rapid effect is required, such as cerebral or spinal syphilis. For this purpose 1 *grain of calomel*, suspended in 10 minims of liquid paraffin, may be injected, and repeated once a week for three or four weeks. Injections of calomel are extremely painful, and more liable than other methods to cause stomatitis and nodosities in the buttocks. The pain generally occurs on the second or third day after injection, and is occasionally accom-

panied by febrile symptoms. Fournier specially recommends calomel injections in the following conditions: Chronic palmar and plantar syphilides, depapillating glossitis, sclerosing glossitis, tuberculo-ulcerative syphilides, tertiary syphilis of the larynx, and phagedena, both primary and tertiary.

Advantages and Disadvantages of Injections. — The treatment of syphilis by mercurial injections is a scientific method which has the advantages of exact dosage, secrecy, and control by the surgeon himself. Injection takes up much less time than inunction, and avoids the revelatory staining of the linen, which is such a drawback to the inunction method.

With regard to the advantage of *exact dosage*, undue importance must not be attached to this point, for the action of mercurial treatment should be estimated by the effects obtained rather than by mathematical precision in dosage. As Fournier says, 'mercury, when properly administered, always enters the system, whatever the method adopted, and the subcutaneous method, from this point of view, is not distinctly superior to any other method.' The injection method has the advantage of leaving the stomach free for the administration of other remedies, but this advantage also applies to the method of inunction.

On the other hand, there are certain *disadvantages* connected with treatment by injection, the chief of which are pain and the formation of nodosities at the point of injection. Abscesses, which used to occur more frequently, are now rare, owing to antiseptic precautions being more generally adopted. Pulmonary embolism has been occasionally reported, but must be regarded as a rare complication. The *pain* of injections varies in different subjects and with different preparations of mercury; it is severe with calomel, perchloride, and benzoate of mercury, but slight in the case of gray oil.

Nodosities of the buttocks are caused by inflammatory exudation around the deposit of mercury. They generally disappear in a few weeks, but may sometimes persist for several months. In some cases amicrobial abscesses form at the point of injection; they are generally superficial, and are found to contain chocolate-coloured, semi-fluid matter when incised.

Fournier mentions a case in which nodosities left after mercurial injections subsequently became the seat of gummatous growths.

Comparison of Soluble and Insoluble Injections.—A list of the chief mercurial preparations used for injection will be found in the Appendix. The *biniodide* appears to be the best, although good results have been reported with benzoate, neutral salicylate, lactate, and hermophenyl. The more recently manufactured mercurial preparations, such as the cacodylate, chloromercurate of ammonium, salicyl-arsinate, and mercurial nucleoproteid, appear to be much inferior to the others in therapeutic effect. The nucleo-proteid, or 'mercurial yeast,' is a preparation extracted from beer yeast gradually accustomed to grow in association with perchloride of mercury. The metal is in a 'dissimulated condition.' This preparation, although of scientific interest, is not of much therapeutic value.

The main objection to *soluble* injections is that, although rapidly absorbed, they are eliminated with equal rapidity, so that they have to be repeated daily or every other day. This fact, combined with their usual painfulness, renders them irksome to both patient and surgeon.

With injections of calomel, or other insoluble salts of mercury, the first part of the dose is rapidly absorbed, and produces an active therapeutic effect, while the remainder remains at the site of injection and is more slowly absorbed, owing to vascular changes around it which hinder absorption. In the case of metallic mercury, injected in the form of gray oil, the absorption is slow and continuous for several days, as is shown by the presence of mercury in the urine. The injection of metallic mercury therefore produces more gradual mercurialization of the organism, and the dose has less often to be repeated.

The fact that part of the dose injected remains for some time at the site of injection has been urged as an objection to the use of insoluble injections, and cases have been reported in which such residual foci gave rise to dangerous symptoms subsequently; but such cases have usually resulted from the injection of unusually large doses.

Intravenous Injections.—This method, which was introduced by Bacelli in 1893, consists in the direct injection of mercurial salts into the blood-stream. It is obvious that soluble preparations only can be used for this method, and the chief ones which have been employed are the cyanide and biniodide.

Technique.—After rendering the skin aseptic, one of the veins at the bend of the elbow is made prominent by compression, and the needle of the syringe is inserted obliquely till its point is felt to be free inside the vein. The compression is then removed, and the solution slowly injected into the vein. The dose is about $\frac{1}{6}$ grain, and the injections are made every other day or daily according to the case.

Advantages and Disadvantages.—The advantages claimed for this method are quickness in absorption, rapid therapeutic effect, and painlessness. The disadvantages are—(1) the difficulty of finding a suitable vein in women and obese subjects; (2) the risk of periphlebitis, thrombosis, and embolism. Moreover, the advantage of rapid absorption is counterbalanced by the equal rapidity of elimination.

An extensive trial has been given to intravenous injections by Barthélemy and others on the Continent, and by Lane in London, but the method appears to have no advantages over intramuscular injection. It may, however, be useful in cases of cerebral and ocular syphilis where an immediate effect is required.

Conclusion.—The value of mercurial injections as compared with other methods of mercurial administration cannot be definitely settled, owing to the comparatively short time during which the injection method has been in vogue. In order to test one method with another it would be necessary to estimate the number of cases of tertiary syphilis which follow in a given number of cases treated by each of the different methods. It is hardly necessary to say that such an investigation would have to extend over many years.

We may conclude (1) that mercurial injections, although they have not superseded the older methods of treatment, constitute a valuable addition to the therapeutics of syphilis; (2) that injections of *gray oil* must be regarded as one of the best

of the routine methods for the treatment of syphilis; (3) that injections of *calomel*, or intravenous injections of *biniodide*, are useful in urgent cases where a rapid effect is required, as in cerebral or ocular syphilis.

An injection of calomel is sometimes useful as a therapeutic test in cases where the diagnosis between syphilis and malignant disease is doubtful.

Fumigation.—This method, which was in former times much in vogue, is seldom used nowadays, but is still carried out in some of the Turkish baths, where a room is kept for the purpose.

The patient is seated on a wooden chair, and enveloped in a sheet which extends from his neck to the floor. The vapourizing apparatus, which consists of a spirit-lamp, tripod, and water-bath, is placed under the chair. About a drachm of calomel is placed in an inner dish in the water-bath and volatilized by the heat of the lamp. In a few minutes the patient is enveloped in an atmospere of steam and volatilized calomel. The sheet is tied carefully round the neck of the patient, to avoid inhaling the vapour. The operation is complete in about twenty minutes, after which the patient is put to bed enveloped in the sheet. The fumigations may be repeated every day or every other day till the required effect is produced.

The only advantage of the method is to cause the disappearance of troublesome and compromising syphilides by rapid mercurialization. The disadvantages are its uncertainty in effect, its liability to cause stomatitis, and the danger of inhaling calomel vapour if it is not properly carried out. A fatal case was reported by the late Henry Lee.

Varia.—Other methods, based on the absorption of mercurial vapour, by wearing a kind of bag of mercurial ointment (Welander), or by cotton impregnated with mercury and placed on the patient's pillow (mercolint), may be mentioned, but these have only a feeble therapeutic action.

With regard to the *relative therapeutic value of the different mercurial preparations*, it is impossible to estimate this factor, because we cannot ascertain the toxic nor the antisyphilitic

equivalents of mercury for each individual, which vary in different subjects, and in the same subject under different conditions. We can only judge the action of mercury by its therapeutic effects. In any case the therapeutic effect does not appear to be proportional to the percentage of mercury in the different preparations.

Iodide of Potassium.

Iodide of potassium has the remarkable power of causing the absorption of syphilitic neoplasms, but it is not by itself sufficient for the cure of syphilis. It is therefore chiefly of use in the treatment of gummatous growths in the later stages of syphilis, and as a therapeutic test in cases of doubtful diagnosis.

Administration.—Iodide is always given by the mouth, except in urgent cases where it cannot be swallowed (cerebral syphilis, etc.), when it may be administered by enemata or by subcutaneous injection.

The drug appears to act better when given in a large quantity of water between meals (½ pint to 1 pint). It is customary to add a decoction of cinchona or carbonate of ammonium to 'counteract the depressing effect of the iodide.' This is, however, not necessary if the dose is given with plenty of water, which may be flavoured according to taste.

Opinions differ with regard to the *dosage* of iodide more than in the case of mercury, and the dose naturally varies according to the severity of the case and the tolerance of the patient. Some patients are more susceptible than others to the toxic effects of iodide, but the average efficacious dose may be stated as 10 to 15 grains three times a day (30 to 45 grains). In severe cases the dose may be increased up to 30 or even 60 grains three times a day, but larger doses than this are unnecessary, and probably have no more therapeutic action than smaller doses.

In administering iodide it is well to begin with a dose of 10 grains, and increase the dose in a few days to 15, and afterwards, if necessary, to 20 grains, three times a day. It is also well to give iodide in short courses of two or three weeks '

duration. If no effect is produced in this time the treatment should be altered, and the drug replaced by mercury. It is common to see hospital out-patients taking iodides for months on end, either through forgetfulness, or because the surgeon has a mistaken idea that iodide has a preventive action on future syphilitic manifestations. This practice is to be condemned, and it cannot be too strongly urged that iodide is only of use in dispersing the present lesions of syphilis, and has little or no preventive action on the future course of the disease. Mercury is the only drug to be relied upon as a preventive against the future phenomena of syphilis, and iodide, although a most valuable accessory, is not indispensable in the treatment of syphilis. This fact was emphasized by Fournier some years ago, but does not appear to be sufficiently recognised.

Substitutes for Iodide of Potassium.—The iodides of sodium and ammonium are sometimes prescribed in place of iodide of potassium, and sometimes all three together; but they have no advantage over the potassium salt. Metallic iodine and certain new preparations, such as *iodipin* and *iodalbacid*, have been tried as substitutes for iodide, but they are all much inferior in therapeutic effect. Considering the remarkable efficacy of iodide of potassium as an antisyphilitic remedy, it seems idle to try and replace it by any of the much-advertised remedies of certain enterprising chemists.

Iodism.—The toxic effects of iodide, known as iodism, vary considerably in different subjects, but appear to be more liable to occur after small than after large doses of the drug. It often happens that when the dose of the drug is increased the symptoms of iodism disappear. The chief phenomena of iodism are coryza and various cutaneous eruptions, which chiefly affect the face.

Coryza.—A slight degree of coryza is common in most subjects who are taking iodide. The symptoms closely resemble those of a cold in the head, but the nasal discharge is more profuse and watery. In more severe cases there is redness and swelling of the eyelids and nose, severe headache, profuse nasal discharge, sore throat, and febrile symptoms,

simulating an attack of influenza (iodic grippe). In rare cases laryngeal and pulmonary œdema may occur. These symptoms develop rapidly, but usually disappear in the course of a few days.

Iodic grippe may lead to errors in diagnosis, especially if the patient is seen by another medical man, who is unaware that he is taking iodide, and cases have been mistaken for influenza, measles, erysipelas, quinsy, etc. Iodic œdema of the larynx may cause urgent dyspnœa and stridor, and in a few instances recorded tracheotomy has been performed. Such cases are fortunately extremely rare.

Cutaneous Eruptions.—The commonest iodide eruption is *acneiform*, usually consisting of a few scattered pustules, but sometimes more extensive and inflammatory. In some cases vesicular, bullous, and rupial eruptions occur, which may occasion considerable difficulty in diagnosis, and the drug may be continued in the hope of curing the eruption it has given rise to. The *rupial iodic eruption* is often extremely difficult to diagnose from syphilitic rupia, and the true nature of the lesion is often only revealed by suspending the drug. The chief points in which the iodic eruption differs from the syphilide are the following: (1) Rapidity of onset, the iodic eruption quickly passing through the vesicular and pustular to the crustate stage, the syphilide being of slower evolution; (2) difference in the initial type, the iodic eruption commencing in the form of vesicles, bullæ, phlyctenules, etc., which are not common in syphilis; (3) the bright red inflammatory areola, which differs from the ham-coloured areola of syphilides; (4) absence of the neoplastic infiltration which is always present at the base of the syphilide.

In some cases the iodide eruption assumes a *tuberous* form, consisting of smooth, oval or circular, raised, condylomatous lesions, chiefly occurring on the face. These lesions are usually the result of prolonged absorption of the drug, and a fatal case has been reported in which this form of eruption resulted from the use of a much advertised 'blood mixture.'

Sometimes the iodide eruption is *vesicular* or *bullous*, forming extensive lesions on the face, neck, and arms. A fatal case

of hæmorrhagic vesicular eruption was reported by Stephen Mackenzie in a child of five months, after a single dose of 2½ grains of iodide only. In some persons iodide gives rise to a *purpuric* eruption of small deep red petechiæ, chiefly affecting the front of the legs.

The effects of iodism may be counteracted to a certain extent by administering 5 minims of *liquor sodii arseniatis* to each dose.

Action of Iodides.—According to Pouchet, iodides act by stimulation of the lymphoid tissue, by a stimulating action on the process of disassimilation, and by an accessory action on the circulation and respiration. Iodide must therefore be regarded as the specific medicament of lymphoid tissue.

Iodides act both by stimulating the means of defence of the organism by provoking leucocytosis, and also by their bactericidal action.

Mixed Treatment.

Some lesions react better to a combination of mercurial and iodide treatment than to either of these drugs alone. Thus, iodide of potassium, which has little effect on early syphilitic lesions, is useful when combined with mercury in the later secondary manifestations, such as the syphilides which are intermediate between secondary and tertiary syphilis; in headache and periosteal pains; in ocular and cerebral syphilis, and in malignant syphilis. On the other hand, mercury is useful in some tertiary manifestations which do not always yield to iodide.

A course of mercurial treatment should always follow the cure of a tertiary lesion by iodides.

Mixed treatment may be given by the mouth in the form of a mixture of *liquor hydrargyri perchlor.* (2 drachms) with *iodide of potassium* (10 to 20 grains) three times a day, but it is much better to combine internal administration of iodide with either inunction or injection.

Auxiliary Medication.

Although mercury and iodide of potassium form the basis of the treatment of syphilis, a good deal can be effected by

auxiliary medication. In the first place, the patient should, if possible, lead a quiet and regular life, free from mental and bodily fatigue and excesses of all kinds. A simple and nutritious diet should be taken, and alcohol of any kind is best avoided during the presence of active symptoms. Alcohol is 'the born enemy of syphilis'; the vascular changes caused by alcohol diminish the resistance of the tissues to specific infection, and in alcoholics mercury and iodides exert only an attenuated action. Quinine and cod-liver oil are useful as tonics, and iron and arsenic should be given if there is much anæmia.

Hydrotherapy is a useful addition to the treatment, either in the form of hot-air or vapour baths, or by treatment at one of the sulphur springs. These measures are especially useful after each mercurial course, as they favour the elimination of mercury and stimulate metabolism generally. A course of treatment at the sulphur springs is indicated in cases subject to frequent recurrences in spite of treatment, and in malignant syphilis.

Serum Treatment.

Various attempts have been made to institute a serum treatment for syphilis, but so far none of these have given much promise.

The first experiments were made by injection of the serum of animals, such as the horse and dog, who were immune against syphilis (Tommasoli). Human serum from the subjects of tertiary syphilis, from cases of secondary syphilis successfully treated by mercury, and from heredo-syphilitic infants, has been employed by Pellizzari, Finger, Landsteiner, and others. Richet and Héricourt made a further modification by using the serum of animals (dogs, goats, and asses) previously inoculated with human serum from cases of primary and secondary syphilis. Tarnowski tried injections of serum from horses which had been mercurialized by injections of calomel, but found that the therapeutic effect on the course of syphilis was nil, and that anæmia and other deleterious effects often followed.

It is unnecessary to give further details of these experiments, as the whole question of sero-therapy in syphilis has been revolutionized by the successful inoculation of monkeys with syphilis by Metchnikoff and others. Metchnikoff has found that certain species of monkeys are more refractory to syphilis than others, and has attempted to obtain a serum from those species which were only susceptible to syphilis in a modified form. This research has, however, not yet given satisfactory results (*vide* p. 41).

General Considerations concerning Treatment.

When should treatment be commenced? This is a point which has been the subject of a good deal of unnecessary controversy. As Fournier points out, the treatment of syphilis should begin *as soon as it is diagnosed.* Although treatment should be postponed in cases of doubtful chancre till the diagnosis is confirmed by the appearance of secondaries, it is difficult to conceive any reason for delay in treatment when the chancre, with its satellite glands, has all the characteristics of typical primary syphilis. It is to be hoped that the search for the *Spirochæta pallida* (if this continues to hold its position as the pathogenic microbe of syphilis) in cases of doubtful chancre will help to put an end to the method of procrastination in the treatment of syphilis which is still practised by certain surgeons.

How long should treatment be continued? In Ricord's time the duration of treatment was usually limited to a year, and consisted of a course of six months with mercury, followed by several months' treatment with iodide. But it is now agreed that this length of treatment is quite inadequate, and most authorities recommend treatment extending over three or four years, with intervals of rest between the successive courses.

Preventive or Chronic Intermittent Treatment.—This method, which was originated by Fournier, consists in successive courses of treatment, with intervals of rest, prolonged over several years. The periods of rest, or suspension of treat-

ment, are gradually increased as the case progresses. The chronic intermittent treatment is distinguished from the continuous and the symptomatic methods. In the *continuous method* treatment is continued without interruption (except in the case of mercurial intoxication) for about two years. The *symptomatic method* consists in confining the treatment to the periods during which active syphilitic manifestations are present.

It has been said by the opponents of the chronic intermittent method that it does not prevent recurrent outbreaks of symptoms. This is an idle objection which applies to all forms of treatment. The great object of the chronic intermittent treatment is to *prevent the development of tertiary syphilis*, and it is demonstrated by the statistics of Fournier, which are the most elaborate that have ever been prepared, that this method is more successful than others in attaining this object. The main objection to the continuous method is that the organism becomes accustomed to the presence of mercury, and the action of the drug becomes thereby diminished. Hence the advantage of the intermittent periods of rest, during which the mercury becomes eliminated from the system. As regards the symptomatic method, this only treats the disease when *patent*, while the chronic treatment treats it when both *patent and latent*, and thus has a better chance of achieving a preventive effect. The chronic intermittent method of treatment, which is now adopted by the majority of syphilologists, must therefore be accepted as the best.

Neisser concludes that the chronic intermittent method is the only one which can lead to the radical extinction of the *Spirochæta pallida*. He also suggests that treatment should be administered by different routes, so as to attack all the foci of spirochætes, and urges that more attention should be paid to localized foci by means of *regional* treatment.

Fournier considers that *four years' mercurial treatment* is necessary for syphilis, and his latest scheme is to divide this into periods, separated by intervals of rest, so as to cover the years during which tabes and general paralysis are most likely to occur. His programme begins with *two years* of chronic intermittent treatment, consisting of courses of treatment of

six weeks' duration, separated by intervals increasing from four to six weeks. After this comes a period of rest for two years, and then a year's similar treatment during the *fifth and the seventh or eighth* years, making four years in all.

As the third year of the disease is the time of maximum frequency for cerebral syphilis, it would appear better to make the initial period of treatment three years instead of two.

It is always advantageous to commence treatment with an energetic course of mercury, and the following modification of Fournier's programme is suggested:

Author's Scheme of Treatment.—1. (*a*) Treatment by *injections of gray oil* for the first six months (whether treatment is begun with chancre or with secondary period). Injections of 1 grain to be given twice a week till active symptoms have subsided (usually four to six weeks); then once a week for the rest of the time, in courses of six weeks' duration, separated by two weeks' intervals of rest. (*b*) Or *inunction* till active symptoms have disappeared, followed by weekly injections of gray oil for the rest of the six months, as above. (*c*) If neither of the above methods is feasible, *blue pill* in doses of 2 grains three times a day, till active symptoms have subsided; afterwards twice a day for the rest of the six months, in courses of six weeks' with intervals of two weeks.

2. After this a month's interval during which treatment is suspended.

3. Continuation of treatment by blue pill (2 grains twice a day) for periods of six weeks, with two weeks' intervals, during the remainder of the first and during the second year.

4. The same courses of pill treatment, with intervals of a month, during the third year.

Suspension of treatment during the fourth year (provided there are no symptoms).

6. A year's treatment as in No. 4 during the fifth and seventh years.

This scheme must not be regarded as absolute, nor as applying to all cases, for every case of syphilis must be treated on its merits, and any scheme of treatment must be modified according to circumstances.

It is obvious that the mercury must be temporarily sus-

pended if stomatitis or other signs of mercurial intoxication occur. Again, if tertiary lesions appear in spite of this prolonged treatment, they must be treated with iodide, followed by a further course of mercury.

It will be noticed that in this scheme the whole treatment is by *metallic mercury*, either in the form of pill, gray oil injections, or inunction. There does not appear to be any advantage in using other preparations, except in cases which are refractory to metallic mercury, and in the author's experience mercury in the metallic form is better tolerated by the majority of patients, and causes less disagreeable symptoms than the other mercurial compounds. With regard to *iodides*, they should be used during the course of treatment according as indications arise for mixed treatment.

The only objection to this programme is the number of years over which the treatment is spread, and for this reason few patients are willing to persevere with it. The average patient, as soon as his first symptoms have disappeared, gives up treatment till some late manifestation occurs, for which he probably blames the method of treatment instead of his own manner of carrying it out. Moreover, many patients are afraid of mercury, and regard it as a bugbear to be got rid of at the earliest possible opportunity, whereas occasional courses of blue pill may be taken for many years without any evil effect, and certainly have a beneficial action on the liver.

As the domain of syphilis is extended by the study of the parasyphilitic affections, and as the number of disorders in which syphilis is found to be an etiological factor continues to increase, so the necessity for more prolonged treatment becomes more and more evident; and, although it may be true, as Gowers believes, that the majority of cases of syphilis become cured, we must admit with Balzer that most patients should be on their guard for the rest of their lives.

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CHAPTER XV

SYPHILIS IN RELATION TO LIFE ASSURANCE AND MARRIAGE

THE question of syphilis and life assurance has become more important by the recognition of syphilis as the chief cause of general paralysis, tabes, and aneurism, and one of the chief factors in arterial and cardiac disease, cirrhosis of the kidney and liver, etc. In fact, the study of parasyphilis has vastly altered the aspect of syphilis from the point of view of prognosis. In the case of syphilis a difficulty arises in the period of health intervening between the early and late symptoms, and this latent period generally exists at the time when persons are anxious to insure their lives.

The points to be considered are—(1) the percentage of syphilitics at the time of insurance, and the number who contract the disease after insurance; (2) the number of cases in which syphilis can be proved as a cause of death, directly or indirectly; (3) the number of cases in which syphilis shortens life, and in what form this occurs; (4) the factors on which the evolution of severe syphilis depends in each case; (5) the signs by which severe syphilis can be expected.

None of these questions can be definitely answered. Only a small proportion of syphilitics acknowledge having had the disease, and some are, no doubt, ignorant of having contracted it. In Berlin it is stated that 24 per cent. of men aged thirty have syphilis. Statistics showing the frequency of tertiary lesions include comparatively harmless ulcerations of the skin along with severe lesions of the central nervous system. In order to ascertain the influence of syphilis on the expectation of life it would be necessary to observe a great number of

individuals, syphilitic and non-syphilitic, living under the same conditions during many years.

Runeberg of Helsingfors has investigated the mortality caused by syphilis among persons assured by the Kaleva Company from 1875 to 1897.

'During this period the number of deaths was 734. Runeberg gives a list of 84 cases (11·4 per cent. of the total) in which death may be regarded as to some extent the result of a previous syphilitic infection. The assigned causes of death in these 84 cases are as follows: Cardiac disease, 31 (including 24 cases of sudden death from *Herzschlag*); general paralysis, 22; other affections of the brain and spinal cord, 21 (including 14 cases of cerebral hæmorrhage or cerebral softening); chronic nephritis, 3; aortic aneurism, 2; arteriosclerosis, 2; "bone erosion," 1; unilateral pulmonary cirrhosis, 1; uncertain tumour of the neck, 1. Runeberg directs especial attention to the relative frequency of fatal disease of the heart and nervous system amongst these cases. In regard to heart diseases, the early recognition of a possible syphilitic factor in its causation is of the greatest importance for treatment. Amongst the 22 cases of general paralysis, a history of syphilis was given in 11 at the time of life assurance; in 5 others medical evidence of syphilis was obtained (in at least 1 of these the syphilitic infection took place after assurance); in 3 others a history of supposed soft chancre was given. Runeberg therefore felt justified in including all the cases, though in the remaining 3 he could obtain no proper evidence of syphilitic infection or of chancre.'

'Of the total 84 deaths, 5 occurred between the ages of 21 and 30; 33 between 31 and 40; 29 between 41 and 50; 16 between 51 and 60; 1 between 61 and 70. The mean age at death was 43·4. The mean interval between the supposed syphilitic infection and death was 20·2 years. The mean interval between life assurance and death was 8·1 years.'

'Runeberg thinks that in reality he has under-estimated the number of cases in which death was more or less consequent on previous syphilitic infection; and as a basis for this supposition he gives a table of forty-seven cases in which there was no

history of syphilis, but in which death occurred under the age of fifty from "heart-stroke," cerebral hæmorrhage, or cerebral softening. He thinks about 75 per cent. of these cases of apoplexy and about 50 per cent. of the "heart-stroke" cases are probably in reality due to syphilitic disease of bloodvessels; and if his view be accepted, the deaths more or less brought about by syphilitic infection amount to 15 per cent. of the total, instead of only 11·4 per cent., as deduced from the first list. *This places syphilis amongst the causes of death next to tuberculosis in frequency*, and above pneumonia, since during the same period 21·3 per cent. of the deaths were assigned to tuberculous affections and 10 per cent. to pneumonia.'

'Runeberg recommends that no life should be accepted within two or three years after syphilitic infection, on account of the special liability to cerebral disease during the first years. Lives should be rejected when there has been any symptom of syphilitic disease of the bloodvessels, even though merely temporary, whether of the nervous system or of the heart. In ordinary cases, however, with a mere history of syphilis, insurance should not be refused, though an extra rating is required, the amount of the extra depending on the length of time which has elapsed since infection, the thoroughness of the treatment, the intelligence of the applicant, and his ability to obtain prompt medical aid should any symptoms occur.'

Tertiary syphilis of the nervous system is often fatal apart from tabes and general paralysis. In cirrhosis of the liver and kidney syphilis it is probably the chief factor in many cases, and a secondary factor in others. Also, the addition of syphilis to tubercle, alcoholism, and malaria renders the prognosis more grave. Finally, syphilis, by diminishing the power of resistance of the organism, renders the effects of all illness and accident more serious.

Byrom Bramwell has investigated the causes of death occurring in the Scottish Widows' Fund. Out of 3,658 deaths which occurred during the seven years 1888 to 1894, 6 were due to tabes, 52 to general paralysis, and 24 to aneurism of the aorta. Granting that 75 per cent. of the 58 deaths due to tabes and general paralysis and 50 per cent. of the 24 deaths

due to aneurism were the result of syphilis, we get 55·5 deaths out of 3,658 cases due to what may be termed syphilitic tabes, general paralysis, or aneurism.

Then, if it is assumed that 20 per cent. of the total 3,658 males had had syphilis, we arrive at the fact that 731 persons who died assured in the Scottish Widows' Fund during the seven years had had syphilis. Therefore, one in 13·1, or 7·5 per cent., of all the syphilitic persons who died insured in this company during the seven years died from tabes, aneurism, or general paralysis. Further, if in each of these the expectation of life was shortened by 18 years, it follows that in every syphilitic person, as above, the expectation of life was shortened by 1·3 years.

Bramwell points out that in addition to the three great causes which he has considered—viz., tabes, aneurism, and general paralysis—there is a further mortality in aortic valvular disease, cirrhosis of the liver and kidney, due to syphilis. Also, many deaths certified as cerebral softening, apoplexy, hemiplegia, paraplegia, insanity, myelitis, angina pectoris, myocarditis, atheroma, laryngitis, etc., must be added to the death roll of syphilis. Finally, syphilitic arteritis tends to shorten life by predisposing to intercurrent diseases.

Tertiary syphilis probably occurs, according to Bramwell, in 10 per cent. of all cases, and if it is granted that in all these life is shortened by ten years, then, on an average, in every case of syphilis life is shortened by one year.

If it is assumed that syphilis is the sole cause of tabes, general paralysis, and aneurism, the shortening of life in syphilis will be about two years in consequence of these diseases alone, and if the other diseases mentioned above are added a figure is reached of about four or five years.

The question of the factors which cause severe forms of syphilis can only be settled by numbers of clinical observations. Among these factors are (1) absence or insufficiency of treatment; (2) combination with alcoholism and tuberculosis; (3) overwork, malnutrition, etc. The worst of these is alcohol. In other cases we must admit a special susceptibility of the organism to syphilis, and in some cases traumatism acts

by setting up periostitis. The idea that mild early symptoms are followed by severe tertiary lesions, and severe early symptoms by mild or absent tertiaries, is probably incorrect. Nonne states that among his cases of late syphilis of the nervous system there was a considerable proportion of severe early symptoms. The truth of the idea would appear to lie in the *neglect of treatment* in the case of mild secondary manifestations.

Neisser shows that out of 500 cases of tabes more than half had undergone no regular treatment, and only 5 per cent. had been through a proper course. Fournier, in his recent remarks on general paralysis at the Academy of Medicine at Paris, showed that four-fifths of the cases had received insufficient treatment.

The influence of race and station in life must also be taken into consideration. It is said that in Norway, Bosnia, Roumania, Turkey, Russia, and other partially civilized countries where syphilis has affected the entire lower classes, tabes and general paralysis are rare, while tertiary symptoms are common. It appears probable that the inhabitants of large cities whose nervous systems are overworked have less resistance to syphilis of the nervous system.

Hence the prognosis in a given case of syphilis depends not so much on the syphilis itself as on the individual—his constitution, habits, and mode of life, and these factors cannot be used in a statistical inquiry.

Concerning the admission of syphilitics to an assurance company, a thorough examination should be made of the nervous and vascular systems. If there is any sign of arteriosclerosis, aneurism, commencing tabes, or general paralysis, they must be refused. Florschutz has reported a series of cases which developed general paralysis shortly after admission to an insurance company. Blaschko advises temporary rejection of cases with recent syphilis, but admission of those with the scars of late syphilis, because the latter may live for years in good health. On the average he thinks a life may be accepted four or five years after the onset of the disease, in the absence of symptoms.

These cases may be dealt with by two methods—(1) by

admitting all syphilitics with extra premium; (2) by admitting at ordinary rates all those in good conditions of life, and in whom there are no accessory conditions, such as alcoholism, constitutional debility, etc., and refusing every doubtful case. Blaschko favours the latter alternative. There is one point to be borne in mind—viz., the impossibility of knowing whether the candidate for life assurance is a syphilitic or not, in the absence of history, signs, or symptoms. History is frequently unknown and more often concealed, and a man in apparently robust health may die suddenly of cardiac or cerebral syphilis shortly after insuring his life.

Syphilis and Marriage.

Medical men are frequently consulted by syphilitic patients as to the advisability or not of marriage, and opinions differ as to the length of time that should elapse before marriage becomes safe. In this country, owing to the doctrines of Hutchinson, there is a prevalent idea that two years is a sufficient interval, and Mr. Hutchinson, as recently as June, 1906, repeated his opinion that 'with reference to marriage, if the treatment has been continued for two years from the date of the chancre, a man may safely marry, but a much longer period is necessary for a woman.'

He also remarked: 'I have let hundreds of such patients marry, and they have never come back to me in consequence of having infected their wives, or of having syphilitic children.' This statement cannot be accepted as evidence of the safety of the two years' system, for, in case of failure, it is probable that the patients would not come back. In this way the successes are recorded but the failures unknown. Unfortunately the medical men who have the greatest opportunities for carrying out observations of this kind—the general practitioners—are often ill-informed on the subject, owing to the total absence of any systematic teaching of syphilology in this country.

Fournier, on the other hand, lays down the law that no syphilitic should marry for at least three or four years after onset of the disease, and then only when the following

conditions are fulfilled: (1) Absence of actual lesions; (2) prolonged treatment; (3) a period of immunity from symptoms for at least one and a half to two years, during which time no treatment has been taken; (4) a benign type of disease. Fournier relates the history of 20 cases of marriage in syphilitics under two years; 19 of the wives were infected, and there were 28 pregnancies, resulting in 13 abortions, 6 early deaths, 6 syphilitic infants, and only 3 healthy children.

Ledermann says: 'Generally speaking, marriage may be allowed if at least five years have elapsed since the infection took place, if no more manifestations have occurred during the last two years, and if the patient has received an energetic and thorough mercurial treatment.'

Prince Morrow states that 'when the syphilitic diathesis has been subjected to the double depurative action of time and treatment during a period of four years, in the vast majority of cases it is scientifically safe for the syphilitic to marry.'

Balzer is of opinion that marriage may be allowed during the fifth year, provided that the symptoms have been benign, the treatment regularly followed, and that there have been no symptoms during the fourth year. He also advises a course of preventive treatment immediately before marriage, and during the year following. In the case of a syphilitic woman preventive treatment is required for a long time, because the power of maternal transmission lasts much longer than that of paternal heredity.

It thus appears that Hutchinson's two-year limit is only half that given by other authorities. Considering that the third year of the disease is the most prolific in tertiary manifestations, it would appear obvious that a two-year limit is absolutely inadequate. Moreover, contagious lesions are known to occur ten years or more after the chancre, even in cases which have been properly treated. Hence any arbitrary time-limit is both dangerous and unscientific.

In forming a conclusion on this subject there are two points to be considered:

In the first place, is it any business of the medical man to 'give his sanction' to marriage at all? Marriage is a civil

contract concerned chiefly with matters other than medical. The duty of the medical man ends with pointing out to his patient the possible eventualities in case of his marriage.

In the second place, marriage is not necessarily synonymous with the procreation of children. If a syphilitic can avoid impregnating his wife there is no reason why he should not marry in the absence of contagious lesions. With regard to the question of child-birth the case is entirely different, for the evils of syphilis are visited far more severely on the children than on the parents, and it is impossible to fix any date at which a syphilitic is free from the danger of transmitting the disease.

If we were authorized to attempt an improvement of the human race by the extinction of syphilis, we should forbid any syphilitic to bear children, which in practice would mean that all syphilitics would be debarred from matrimony. Such a state of affairs is obviously Utopian, and the only duty of the medical man is to carefully explain the situation to his patient.

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CHAPTER XVI

HEREDITARY AND CONGENITAL SYPHILIS

SYPHILIS is the hereditary disease *par excellence*. Its hereditary effects are more inevitable, more multiple, more diverse, and more disastrous in their results on the progeny and the race than in the case of any other disease. Syphilis, in fact, has a more harmful influence on the species than on the individual.

Hereditary syphilis appears to have been first mentioned by Paracelsus (1529), who wrote: '*Fit morbus hereditarius, et transit a patre ad filium.*' It was described by Ambroise Paré, who in 1633 wrote: 'Souvent on voit sortir les petits enfants hors le ventre de leur mères ayant cette maladie, et tôt après, avoir plusieurs pustules sur leur corps; lesquels estant ainsi infestés, baillent la vérole à autant de nourrices qui les allaitent.' Ambroise Paré hence recognised the possibility of contagion by suckling.

From the time of Paré hereditary syphilis has been the subject of innumerable writings and much controversy, especially with regard to the question of paternal or seminal transmission.

Transmission to Fœtus.

First of all, it is necessary to distinguish between true *hereditary syphilis* and *congenital syphilis*. The latter embraces all cases which show signs of syphilis at or soon after birth, and includes cases where the mother has been infected during pregnancy, or *post-conceptional syphilis*. The term 'hereditary syphilis,' used in its strict sense, only applies to cases of infection of the ovum by maternal syphilis, or by transmission of infection to the ovum by the spermatozoa of the father—in other words, *germ* or *sperm* infection (ovular or spermatic).

This distinction, although difficult to establish clinically, is important from the pathological point of view; for it is obvious that infection of the ovum will cause more damage to the product of conception than infection of the fœtus at a later date through the placental circulation (placental transmission). It is also apparent that the results must differ according to the state of development of the fœtus at the time of infection. Thus, malformations of the fœtus, arrests of development of different organs or of the fœtus as a whole, are probably due to ovular infection; while infection at a later stage of development will cause the ordinary heredo-syphilitic lesions of the different tissues and organs.

Transmission of syphilis to the fœtus may thus take place in three ways—(1) from both parents, constituting mixed transmission; (2) from the mother alone; (3) from the father alone.

Mixed Transmission.—This takes place when both parents are affected with syphilis at the time of fecundation. In such conditions the fœtus is more likely to be infected than when one parent only is syphilitic. According to Fournier, the morbidity of mixed transmission is 92 per cent. and the mortality among the infants 68·5 per cent.

Maternal Transmission.—This includes both ovular or germ infection and placental transmission during pregnancy, or both hereditary and congenital syphilis. Fournier gives the morbidity as 84 per cent. and the mortality as 60 per cent.

Paternal Transmission.—In this case the father only is syphilitic, and the ovum is infected by the sperm of the father. The morbidity is given as 37 per cent. and the mortality as 28 per cent. by Fournier. Paternal transmission is therefore less harmful to the fœtus than either maternal or mixed transmission.

The question of paternal transmission has been the subject of many and prolonged controversies. Although the clinical evidence is in favour of paternal transmission, it is impossible to determine in how many cases this occurs without infection of the mother.

The chief argument in favour of paternal transmission is the fact that after a series of abortions or syphilitic infants a healthy child may be born after mercurial treatment of the father only. Many facts of this kind have been reported by Fournier, Kassowitz, Hochsinger, Neumann, and others. Cases have also been observed where a woman gave birth to syphilitic children by one man and afterwards healthy children by another.

The arguments brought forward by the opponents of paternal transmission are — (1) that the semen is not inoculable; (2) that the mother of a syphilitic infant is herself syphilitic, as shown by her immunity to infection, known as *Colles's law.*

The first argument, which was based only on the negative experimental inoculations of semen made by Mireur (p. 17), has been demolished by the researches of Neisser and Finger. Neisser showed that the testicles of syphilitic monkeys gave positive results when inoculated in chimpanzees, and Finger successfully inoculated a chimpanzee with semen from a man with secondary syphilis (*vide* Chapter III.).

Clinical evidence also supports the view of infection by the semen. Jesionek reported the case of a medical man who contracted a digital chancre, followed by secondary syphilis. After four months' inunction treatment all symptoms of syphilis disappeared, but the patient nevertheless infected his wife, who developed a vulvar chancre. As there were no syphilitic lesions present in the man at this time, after careful examination, it was concluded that infection took place through the semen. The frequency of vulvar chancres and the rarity of extragenital chancres in women also support this idea, for it is not usual for a man with a chancre or secondary lesions of the penis to have connection, and secondary lesions within the urethra are probably uncommon. It would therefore appear likely that infection often takes place by the semen.

Hochsinger records observations on 72 families in which the fathers were syphilitic, but the mothers showed no sign of syphilis during periods of 4 to 19 years, although they were repeatedly examined (50 cases were under observation for more than 6 years). The 72 mothers gave birth to 276 children—

110 still-born, 166 syphilitic, and 31 healthy. The healthy children were all the last born, except in 4 cases.

Other objections which have been raised against seminal infection are—(1) that the syphilitic microbe cannot be conceived as capable of entering the spermatozoon, which only consists of a nucleus-like body and a tail; (2) that if it did so it would inevitably kill the spermatozoon; (3) that if the syphilitic spermatozoon reached the ovum it would destroy it and prevent development of the embryo.

All these objections are, however, purely theoretical, and we know now that inoculation of semen has caused syphilis in monkeys. There is no need to suppose that the spirochæte actually penetrates the spermatozoon—in fact, it is much too large to do so.* It may travel in the fluid part of the semen, or may attach itself to the spermatozoa, as it has been seen to attach itself to the red blood-corpuscles (Rille and Vockerodt).

The observations of Levaditi show that the spirochæte is present in the fœtal tissues in cases of paternal and maternal transmission by sperm and germ infection respectively. In six observations in which spirochætes were found in the fœtus the mother was previously syphilitic in two cases and the father in one; in one case the mother developed syphilitic symptoms during pregnancy (probably syphilis by conception and paternal transmission); the other two cases were doubtful.

These observations appear to demonstrate that the spirochæte can infect the ovum either by germ or sperm infection, and that the embryo can develop in spite of it, and produce a fœtus whose tissues contain spirochætes in great quantities. Whether this organism can pass the placental barrier is not shown by Levaditi's cases, since there was no distinct case of post-conceptional infection of the mother reported. However, Strauss and Chamberland have shown that anthrax bacilli can pass the placenta, so there is no apparent reason why the spirochæte cannot do the same.

* The size of the head of the human spermatozoon is given as $\frac{1}{22}$ or $\frac{1}{33}$ of an inch (Carpenter), while the spirochæte averages about $\frac{1}{4000}$ of an inch.

We may therefore assume that the *Spirochæta pallida* may infect the ovum, either through previous syphilis in the mother or by the semen of the father; and also that, in some form or another, it can pass the placental barrier and multiply in the fœtal tissues.

As Fournier points out, the denial of spermatic infection is a dangerous doctrine, as it opens the door of marriage to many syphilitic men hitherto deterred by fear of injuring posterity.

Conceptional Syphilis.

Syphilis by conception (the *choc-en-retour* of Ricord and Diday) means infection of a previously healthy mother from a fœtus syphilized by spermatic infection from the father. The occurrence of conceptional syphilis, which has been much disputed, depends on the fact of spermatic infection of the ovum, and as this has been proved to be possible by Finger's demonstration of the contagious properties of the semen, we may also accept the possibility of syphilis by conception.

A case recently reported by Jesionek appears to be an illustrative example of conceptional syphilis and paternal transmission:

A girl of eighteen was admitted to hospital for gonorrhœa, and was kept under close observation during several months. No sign of syphilitic chancre was found, but five months later secondary syphilis developed, the girl being then about five months pregnant. A still-born fœtus was born during the eighth month, with extensive syphilitic lesions of the viscera and bones. This appears to be a case of conceptional syphilis, since no other source of infection was found. The advanced state of syphilitic disease in the fœtus suggests paternal transmission, since it is improbable that such extensive lesions would have developed during two and a half months on the supposition that infection of the fœtus was derived from the mother's syphilis. Jesionek also thinks it probable that direct infection may take place by the semen, because it is rare for a man with a chancre to have connection, and secondary lesions of the penis are uncommon.

Fournier has collected fifty cases which he considers proved to be conceptional syphilis, and he regards this mode of infection of the mother as common in young married couples. Hence a young wife may be syphilized early in pregnancy, and the only evidence of this may be an abortion. According to Fournier, conceptional syphilis is characterized by severe headache, which may be taken for migraine or neuralgia. Therefore, severe headache accompanied by sore throat, etc., in a young married woman should draw attention to the possibility of conceptional syphilis.

Experimental evidence is also in favour of conceptional syphilis. The experiments of Charrin on the passage of the toxins of diphtheria show that these toxins when deposited in the fœtus, either directly or indirectly through the sperm of the father, can be transmitted to the mother, and that if they do not pass in great quantity immunization of the mother may occur as in Colles' law. Guinard has also shown that rose aniline trisulphonate of soda passes from the fœtus to the mother, and can be found in the maternal urine and in the blood. This does not occur if the fœtus is dead.

It is therefore reasonable to suppose that both syphilitic toxins and antitoxins may pass from the fœtus to the mother.

Ballantyne regards conceptional syphilis as 'outside the ordinary physiological laws of transmission,' since it implies such a circuitous route, from the sperm to the ovum, from the ovum to the fœtus, and from the fœtus to the mother. In the light of recent research on the spirochæte, however, this is not so difficult of comprehension, for the long period during which this organism can be latent has been demonstrated by the discovery of spirochætes in tertiary lesions as long as twelve years after infection (Schaudinn). This may explain cases in which the mother receives syphilis in a latent form from the fœtus and develops tertiary lesions some years later —*delayed conceptional syphilis.*

Further research may demonstrate the presence of the *Spirochæta pallida* in the mother in cases of conceptional syphilis, showing that this organism in some phase of its life-history can pass the placental barrier in both directions.

Transmission of Immunity (Colles' and Profeta's Laws).

In 1837 Colles of Dublin pointed out that the mother of a syphilitic infant, procreated by a syphilitic father, was herself immune against infection, and could suckle her child with impunity; while a healthy wet-nurse could contract a chancre of the nipple by suckling the same child. The same fact was demonstrated by Baumès of Paris, about the same time. Hence the term 'Colles' or Baumès' law.'

Profeta's law is the converse of this, and states that the apparently healthy child of a syphilitic mother could be suckled by its mother or by a syphilitic wet-nurse without contracting syphilis. This law has been extended to mean that children born of syphilitic parents are immune against syphilis—an idea which is disproved by the occurrence of reinfection of heredo-syphilitic subjects with acquired syphilis, constituting the *binary syphilis* of Tarnowsky.

The negative results of experimental inoculation by Caspary and Neumann of mothers of syphilitic children is in favour of Colles' law of immunity. On the other hand, cases of exception to this law have been published by Finger, Ogilvie, and others, where mothers contracted chancres of the nipple by suckling their syphilitic infants. However, Professor Fournier, in the whole of his long experience, states that he has never seen a case of exception to Colles' law. It is possible that some cases of so-called exceptions to this law may have been instances of acquired syphilis in the infant soon after birth.

Hence there are two modes of conceptional infection: one which manifests itself during pregnancy by visible lesions—*syphilis by conception;* another which remains latent and only manifests itself by tertiary lesions some years later, as *latent conceptional syphilis.* The latter explains the immunity of the mother, known as the Colles' or Baumès' law.

According to Fournier, the most probable hypothesis is a difference in the *quantity of the virus* in syphilis by conception and latent conceptional syphilis—a large quantity of virus causing syphilis by conception, and a small quantity latent conceptional syphilis with immunity to infection.

In the present state of our knowledge we may assume—(1) that the mother of a syphilitic fœtus is inoculated from this fœtus with an attenuated and latent form of syphilis; (2) that this may remain latent for several years, after which tertiary syphilis may or may not appear (delayed or latent conceptional syphilis); (3) that during this latent period the mother is immune to further infection in most, if not in all cases (Colles' law); (4) that the apparently healthy child of a syphilitic mother may acquire immunity for a limited period, but that in most cases it is in reality infected with latent or delayed heredo-syphilis.

Syphilitic Twins.—Cases have been reported where one of twins developed signs of heredo-syphilis at birth or soon afterwards, while the other apparently escaped infection. Such cases, however, require careful observation for many years before they can be accepted, and the majority are explained by the fact that the infants are observed by one physician for a short time only after birth, and by another in childhood and adolescence.

Barthélemy relates a remarkable case, which illustrates this point and shows how the signs of heredo-syphilis may be delayed for many years in one of twins, while the other shows early signs of the disease.

In Barthélemy's case one of the twins died of syphilitic meningitis at thirteen months; but the other, a girl, showed no signs of syphilis till the age of twenty, when she developed a gumma of the leg. This case was under continuous observation by Barthélemy, who states that the girl was a virgin, and therefore regarded the gumma as due to heredo-syphilis, and not acquired.

It is theoretically possible that in the case of binovular twins the spermatozoon might convey the spirochæte to one ovum only, but such an idea is somewhat transcendental.

The existence of two separate placentas, in the case of post-conceptional infection, will hardly explain the difference in infection of the two twins, since both must receive the infected blood of the mother. It is more probable that one fœtus is more vigorous than the other, and manufactures more anti-

toxic substances or alexines; but it is extremely unlikely that one fœtus ever escapes altogether if the other is syphilitic.

As Eustace Smith points out, 'in the case of twins born of healthy parents we often find one to be more vigorous than the other, and it often happens that one will sink and die, while the other remains strong and robust. So in the case of the inheritance of a constitutional disease, if the twins are, while in the womb, of unequal vigour, the one drawing to itself a greater proportion of nutritive material than the other, the less vigorous fœtus would no doubt have a less degree of resisting power, and would suffer to a greater extent than the other from the effects of a poison to which both are equally exposed.'

Modifications in the Hereditary Influence.

The two chief factors in attenuating the effect of the hereditary transmission of syphilis are the effects of *time and treatment*. Time attenuates and finally annihilates the power of transmission of the syphilis of the parents to the fœtus. At first abortions occur; then stillbirths; then living children affected with heredo-syphilis; finally healthy children. This is known as 'Diday's law of decrease.'

The maximum effect of the hereditary influence occurs in the first year of the parental disease, which Fournier aptly terms the 'year of terror.' Out of 176 cases of stillborn syphilitic infants, 139 were born in the first three years of the parental disease, and 88 of these in the first year.

It is impossible to fix a time-limit to the power of transmission. Out of 562 of Fournier's cases, 60 occurred after the sixth year of the disease, and one as late as the eighteenth year.

The power of hereditary transmission persists much longer in women than in men. Lesser explains this by the fact that there is in man a constant renewal of the spermatozoa, while in women the ova are already formed at birth, and are not renewed. The ova are good storage-places for morbid poisons (Hutchinson).

The beneficial effect of *treatment* is shown by the procreation of a healthy child by treatment of the parents after a series of

abortions. Fournier has noted cases where parents have had healthy children while under treatment, and syphilitic children when treatment was neglected. The production of healthy children after treatment of the syphilitic father is, as we have mentioned above, one of the chief arguments in favour of paternal heredity. Exceptions may occur to the rule of attenuation by time and treatment, and the first children may be apparently healthy, while the latter ones are syphilitic. This is explained by *relapse of the disease in one of the parents.* Hence the popular idea that the birth of a healthy child in a syphilitic family signifies the termination of the disease is not always true. There are some cases of syphilitic heredity which resist the combined effect of time and treatment.

On the other hand, syphilitic subjects may have apparently healthy children, and develop active manifestations after birth of the child. Fournier has collected thirty-five cases of this kind in which the fathers had active syphilis, but the children were apparently healthy. The word 'apparently' is used advisedly, for there is always the possibility of *latent delayed heredo-syphilis*, which may not appear till puberty or adolescence. It is also known that *visceral heredo-syphilis may be present without any cutaneous manifestations* (Neisser, Hochsinger

The *quality of the parental disease* does not appear to have much relation to the effect of transmission to the fœtus. Benign syphilis in the parents is no guarantee of benignity in the hereditary consequences, for it is common to see syphilis of medium severity in the parents produce disastrous effects on the child.

Again, although syphilis is more likely to be transmitted at a time when there are active symptoms in one of the parents, it is not uncommon for transmission to occur when the parental disease is *latent*, even after several years.

Alternating Transmission.—It sometimes happens that a healthy child is born in the middle of a series of syphilitic infants or abortions. Apart from the effect of treatment, which we have just considered, this may be explained by a recrudescence of the disease in one of the parents, or more probably by an *intervening genitor.* In other words, if a really healthy

child is apparently born of syphilitic parents it would appear probable that it has been procreated by another man free from syphilis.

Hochsinger states that alternating heredity is very rare, and he has only seen four cases in which a healthy child was born in the middle of a series of syphilitic pregnancies, out of several hundred observations. He attributes these cases to an intervening genitor.

Post-Conceptional Syphilis—Congenital Syphilis of Infants.

When the mother contracts syphilis during pregnancy the fœtus has a better chance of escaping infection than in the case of ovular or spermatic infection, and the danger is less the later in pregnancy the infection occurs. Transmission to the fœtus in this case seldom occurs when the mother is infected in the eighth or ninth month of pregnancy, but Reiss has reported a case where the fœtus was infected in the ninth month.

In post-conceptional syphilis the virus may give rise to abortion by causing morbid changes in the placenta; or, if it passes the placental barrier it may cause death of the fœtus *in utero*; or a syphilitic child may be born.

Most abortions are due to syphilis contracted before pregnancy; a syphilitic woman who becomes pregnant is more likely to abort than a pregnant woman who becomes syphilitic.

Effects of Syphilitic Heredity.

The effects of syphilitic heredity may be classified as follows:

1. Manifestations of active or virulent syphilis.
   - (*a*) Fœtal syphilis and syphilis of the newly born.
   - (*b*) Early hereditary or infantile syphilis.
   - (*c*) Late or delayed hereditary syphilis.
2. Syphilotoxic or dystrophic manifestations (congenital malformations, arrests of development, general toxic effects, and morbid predispositions), constituting *heredo-parasyphilis*.

Fœtal Syphilis and Syphilis of the Newly Born.

Heredo-syphilis is the chief cause of *abortion*. This occurs more frequently in heredo-syphilis of maternal origin, especially in preconceptional syphilis of the mother (ovular infection).

Fournier gives the mortality among syphilitic infants as 71 per cent. in private and 86 per cent. in hospital practice. The record case is reported by Ribemont Dessaignes, concerning a woman who contracted syphilis from her husband and was not treated. She had nineteen pregnancies, resulting in five stillbirths and fourteen infants which died under six months of age.

The fœtus is frequently *macerated*, or may succumb in the later months of pregnancy to disease of the viscera. When it is born alive with signs of syphilis, it may die from the altered conditions of environment, chiefly concerning the altered conditions of respiration and circulation—that is to say, an amount of disease compatible with life under intra-uterine conditions is incompatible with extra-uterine life. Some newly-born infants succumb to intestinal hæmorrhage associated with purpura (*syphilis hæmorrhagica neonatorum*).

The newly-born syphilitic infant has been described as a 'small, wizened, atrophied, puny, weakly, sickly creature,' with a senile and decrepit appearance. It has been likened to a monkey or a little old man. The skin is flabby, wrinkled, and bistre-coloured. The complexion was compared by Jenner to *café au lait*. In cases of this type there are usually palmar and plantar squamous or bullous syphilides and epiphysitis.

Pathology of Fœtal Syphilis—*The Placenta.*—The syphilitic placenta is larger and more friable than normal, of a pale red colour with yellowish-white patches. Its weight is about one-quarter that of the fœtus, while the normal ratio is about one-sixth.

There is diffuse endo-periarteritis, especially affecting the vessels of the chorionic villi; the latter are hypertrophied and affected with fibrous changes. According to Fraenkel the changes in the placenta vary according to the parental origin of

the disease. He stated that if the syphilis was of paternal origin, the fœtal placenta was affected with hypertrophy of the villi and obliteration of the vessels; if the syphilis was of maternal origin, there was gummatous placental endometritis. Schwab, however, who has recently investigated the subject, finds diffuse changes affecting both parts of the placenta, and regards them as irrespective of the maternal or paternal origin of the disease. Hæmorrhages may occur in the placenta, causing partial separation.

Syphilitic arteritis is also found in the vessels of the *umbilical cord*, causing thickening and obliteration. The placenta and umbilical cord form the first line of defence against contamination of the fœtus from the maternal circulation, and hence bear the brunt of the attack. Hence the frequency of abortion owing to syphilitic disease of the placenta.

The Liquor Amnii.—Hydramnios is of common occurrence in fœtal syphilis. It may be regarded as due to increased pressure in the umbilical vein caused by lesions in the placenta, cord, or liver, and comparable to portal ascites.

The Liver.—The liver in fœtal syphilis is enlarged, hard, and elastic, with rounded margins, and heavier than normal. On section it is of a pale yellow colour (flint liver), and studded with opaque white spots resembling grains of semolina.

Microscopically, there is found to be infiltration of embryonic tissue, leading to fibrosis and endo-periarteritis of the vessels. The semolina grain bodies are miliary gummata, and larger gummata are also sometimes found. There may also be perihepatitis, obliteration of the bile-ducts, and changes in the hepatic artery and portal vein.

The fibroid infiltration develops not only along the portal vessels, but also extends between the groups of cells (pericellular fibrosis), causing more or less atrophy of the hepatic cells. The combined processes of interstitial fibrosis and miliary gummata may affect the whole organ or circumscribed areas only.

The Lungs.—Two conditions have been described as occurring in the lungs of syphilitic fœtuses—(1) 'white pneumonia,' in which the air vesicles are filled with epithelial cells in a

state of fatty degeneration; (2) miliary gummata associated with diffuse fibroid infiltration of the lung.

The Heart and Vessels.—Bar and Tissier have shown that there is a general and widespread process of endo-periarteritis in cases of fœtal syphilis, affecting the larger vessels and those of the viscera. In the heart miliary and also larger gummata have been reported. Diminution in hæmoglobin and poikilocytosis of the red blood-corpuscles have also been described.

The Kidneys.—The changes found in the kidneys consist in fibroid infiltration and endo-periarteritis chiefly affecting the vessels of the cortex.

The Spleen.—This organ is nearly always enlarged. The veins are dilated, and the arteries affected with endo-periarteritis.

The Thymus.—Degenerated gummata and small abscesses have been described.

The Pancreas and Suprarenal Organs.—In both of these there occurs embryonic cell infiltration and endo-periarteritis, resulting in connective-tissue hyperplasia and atrophy of the gland cells.

The Testicles.—These are also affected with fibroid infiltration, resulting in compression and subsequent atrophy of the seminiferous tubules.

The Nervous System.—The brain being still in a state of incomplete development even at the end of fœtal life, the effect of the syphilitic virus is to cause anomalies of construction rather than diseased conditions. These structural anomalies may take the form either of malformations of the brain or of incomplete development. The spinal cord is more fully developed at birth, and may be affected with diffuse meningo-myelitis (Gilles de la Tourette).

The Skeleton.—This may be affected either with malformations or disease. The chief morbid condition affects the *epiphyses* in the form of osteochondritis (or syphilitic epiphysitis). On section of the bone an irregular yellow band of tissue is found separating the epiphysis from the diaphysis. In the normal fœtus this is absent. This yellow zone is due to

fatty degeneration of the newly-formed cells between the cartilage and the bone. This condition may lead to separation of the epiphysis after birth.

The Skin.—The usual cutaneous affection found in the syphilitic fœtus is pemphigus of the soles and palms. The bullæ are large, and contain sero-purulent or sanious fluid. After rupture they leave dark red excoriated surfaces. The later erythematous and papular syphilides of heredo-syphilis are seldom present at birth.

Dystrophies.—'The dystrophies (of heredo-syphilis) are the result of the action of the syphilitic poison upon the organism during the embryonic stage of antenatal life (the first six weeks), or upon such of its organs and tissues which during the fœtal, and even the postnatal, period are still in the embryonic or formative condition' (Ballantyne).

The dystrophies during the embryonic period, which is constituted by the first six weeks of fœtal life, will be severe, and will cause such deformities as hare-lip, cleft-palate, imperforate anus, or may result in the formation of monstrosities. The organs which are developed later on in fœtal life—the skin, eye, ear, brain, skeleton, limbs, and genital organs—will be affected later by the dystrophic action. Later on still the teeth will be affected, as the development of these continues till after birth.

This explains how so many and diverse effects may be caused by the same virus, acting on the organism at different periods of its evolution. Both dystrophies and ordinary syphilitic processes may occur at the same time, the latter affecting the organs or tissues, the development of which is complete.

Bacteriology. — Levaditi has recently demonstrated the presence of the *Spirochæta pallida* in various heredo-syphilitic lesions. His method of staining is given in the Appendix.

In the *liver* numerous spirochætes were found along the intralobular capillaries, in the portal spaces, in the blood-vessels and lymphatics, and also within the liver cells. The organisms were especially numerous round the vessels, and were found in the walls of the vessels and between the endo-

thelial cells of the tunica intima. In the *lung*, affected with 'white pneumonia,' spirochætes were found around the vessels and in the pulmonary alveoli. In some cases the spirochætes were phagocyted by the large mononuclear leucocytes. In the *spleen* spirochætes were found in and around the vessels. In the *kidney* the organisms were present both in the interstitial tissue and within the cells of the convoluted tubules. In the *suprarenal glands* numerous spirochætes were present in the spaces separating the connective tissue of the cortical stroma. The organisms were also found within the cells of the medullary zone. In the *pemphigoid syphilide* spirochætes were found in the bullæ and in the subjacent papillæ of the dermis. They were also present in the sweat glands. Spirochætes were also found in the heart blood, in the thymus, in the medulla of bone, and in the brain and meninges (Ravaut).

It thus appears that the *Spirochæta pallida* is found in greatest abundance in the viscera which are known to be chiefly affected by heredo-syphilis—viz., the liver, lung, suprarenal organs, and the skin; they are rare in viscera which preserve their normal aspect, such as the brain and kidney. This fact negatives the idea that the spirochætes are a form of secondary infection. Moreover, these organisms were found by Levaditi both in infants who presented no external signs of heredo-syphilis at birth as well as in the macerated fœtus.

In acute and fatal forms of heredo-syphilis the spirochætes were more diffused; in later cases more localized, especially in the liver. Hence there may be visceral lesions preceding external signs of heredo-syphilis for some time.

The liver, being the first organ to receive the blood from the placenta, is the most likely organ to be affected in heredo-syphilis of maternal origin.

In the *placenta* the spirochæte has so far only been found in cases where the fœtus was obviously syphilitic. Examination of the placenta for spirochætes has therefore proved of no value in the diagnosis of doubtful cases of heredo-syphilis. Further researches may, however, give better results.

Early Hereditary or Infantile Syphilis.

The classical appearance described above is, however, by no means constant, and in many cases (probably the majority) the infant has no visible signs of syphilis at birth, and may even appear plump and healthy. In these cases the first signs are often *loss of weight and marasmus*. A healthy infant, after losing weight for the first few days after birth, regains this loss and continues to increase after the first week. The syphilitic infant, on the other hand, loses about twice as much weight as a healthy infant, and takes several weeks to regain it. This loss of weight is of great diagnostic value, and when it occurs in spite of proper feeding is strongly suggestive of heredo-syphilis. Another diagnostic point is that the loss of weight often ceases with mercurial treatment. Infants often die of this marasmus, or *syphilitic cachexia*, without presenting any cutaneous syphilitic lesions.

The characteristic symptoms which appear during the first few weeks are—extreme *wakefulness at night*, possibly due to pains in the bone, similar to the ostealgia of acquired syphilis; a *hoarse and aphonic cry; snuffles* (syphilitic rhinitis); *scaly syphilides* round the mouth and on the forehead, eyebrows, buttocks, palms, and soles; *mucous patches* inside the mouth and at the commissures of the lips; *enlarged spleen;* and sometimes enlargement of the liver. The spleen is almost always enlarged in early heredo-syphilis, and in many cases can be felt below the ribs. These symptoms vary in their date of appearance, but generally occur during the *first three months*.

Other manifestations of early heredo-syphilis which may appear during the first few months are—hydrocephalus and microcephalus; otitis media, complicating snuffles; syphilitic deafness, which leads to deaf-mutism; syphilitic meningitis, often mistaken for tuberculous meningitis; orchitis; nephritis; syphilitic dactylitis, frequently mistaken for tuberculous dactylitis; laryngismus stridulus, generally attributed to rickets; epiphysitis; Parrot's cranial nodes; and craniotabes.

Early heredo-syphilis is subject to frequent *relapses*, probably owing to the fact that treatment is not continued long enough.

Donkin mentions the case of an infant with snuffles, scaly syphilides, and laryngitis, which recovered quickly under mercurial treatment, but was brought back three months later with craniotabes, which was not present on the first occasion. In some cases the symptoms are seen to recur from infancy to childhood when kept under observation, and this is probably the case in most cases of apparently late heredo-syphilis.

Late Heredo-Syphilis.

This term is applied to a series of phenomena caused by heredo-syphilis, which appear during childhood, puberty, adolescence, and even adult age. It is doubtful if these cases often occur without any signs of heredo-syphilis in infancy, and they are mostly explained by the earlier symptoms having been either unrecognised or unrecorded. As Hochsinger and others have pointed out, heredo-syphilis may cause visceral lesions without any external manifestations of the disease.

Late heredo-syphilis is probably due, to a great extent, to insufficient treatment of infantile syphilis.

Late heredo-syphilis may appear between the third and twenty-eighth years, the year of greatest frequency being the twelfth. Authentic cases after the twenty-eighth year are rare, but Fournier has recorded three cases at the ages of forty-four, forty-seven, and fifty-seven respectively. It is possible that these were cases of reinfection of a heredo-syphilitic with the acquired disease (binary syphilis of Tarnowsky), but Fournier is rather sceptical with regard to the question of reinfection in syphilis, and regards it as very rare.

Late heredo-syphilis is manifested (1) by syphilitic lesions, mostly of a tertiary nature; (2) by arrested development of organs, or of the body as a whole, causing *infantilism*; (3) by heredo-parasyphilis. Arrested development affects the *teeth*, which are late in eruption, and the power of *locomotion*, which is acquired later than usual. The power of *speech* is also slow in development.

The typical heredo-syphilitic is of stunted growth, with an earthy complexion, depressed or 'saddle-back' nose, square or natiform skull, and notched teeth. Remains of interstitial kera-

titis and radiating scars round the mouth are characteristic signs. The French authors give the name 'triad of Hutchinson' to the three signs—interstitial keratitis, notched or Hutchinson's teeth, and deafness; but both the saddle-back nose and the radiating scars round the mouth are much more common than the true syphilitic deafness.

Other typical signs of late heredo-syphilis are the curved or *sabre-blade tibia*, *choroido-retinitis*, and *atrophy of the testicles*. In doubtful cases the presence of *cicatrices* on the buttocks and thighs and on the palate or pharynx are useful in settling the diagnosis. The scars on the skin are of circular or serpiginous outline, and often consist only of white patches, without any depression or pigmented areola.

The various phenomena of early and late heredo-syphilis are dealt with more in detail in the subsequent chapters.

Heredo-Parasyphilis.

This term includes the dystrophic and syphilo-toxic effects of heredo-syphilis.

The term 'parasyphilis' appears to be subject to various interpretations, and includes the remote sequelæ of syphilis, such as tabes, etc., dystrophic effects, and predisposition to other diseases. It would appear better to apply the term *quaternary syphilis* to actual lesions, such as tabes, general paralysis, leucoplasia, etc., and reserve the term *parasyphilis* for the degenerative effects (dystrophies) and morbid predispositions, or the creation of a soil which is vulnerable to other morbid influences, such as tubercle, rickets, etc.

Dystrophic Effects.—These may be—(1) *general dystrophies*, affecting the organism as a whole; (2) *partial dystrophies*, affecting one system or organ of the body; (3) dystrophies causing *monstrosities*.

General Dystrophy in the fœtus corresponds to the fœtal cachexia which we have previously considered. It frequently causes death by toxæmia, vascular changes, and arrested development of the viscera. When the infant is born alive it is puny, weakly, and stunted, and often dies soon after birth. In children who reach puberty general dystrophy manifests

itself as *infantilism*, with retarded development of the teeth and genital organs, small stature, and general feebleness.

General heredo-syphilitic dystrophy also causes *predispositions* to other morbid influences, such as rickets and tuberculosis. The combination of heredo-syphilis and tuberculosis, or the implantation of tubercle on a heredo-syphilitic soil, explains many cases vaguely referred to as 'scrofulous' or 'strumous' (Ricord's 'scrofulo-syphilis'). It is also conceivable that heredo-syphilitic dystrophy, by affecting the thyroid gland during its development, may cause *cretinism*, and that *myxœdema* may be a manifestation of late heredo-syphilis of the thyroid gland Hertoghe has reported several cases of myxœdema which developed in syphilitics.

Giantism and Dwarfism are probably due in most cases to heredo-parasyphilis. Dwarfs include (1) the so-called 'rickety' dwarfs, caused by arrested growth of the epiphyses; (2) cretins; (3) true dwarfism or *microsomia*, which may be fœtal or postnatal. It is more rational to attribute these cases to hereditary disease than to the so-called 'maternal impressions' or to trauma during pregnancy.

PARTIAL DYSTROPHIES. — These have been extensively studied by Edmond Fournier, who includes among the dystrophic stigmata of heredo-syphilis the following conditions:

1. *Cranial Malformations.*—Asymmetry of the skull, microcephalus and hydrocephalus; acrocephaly and dolichocephaly; synostoses (synostosis of the basi-occipital and basi-sphenoid occurs in cretinism); high arching of the palate; and malformations of the jaws including prognathism.

2. *Dental Dystrophies.*—Retarded development of the first dentition; the various forms of dental malformations, and predisposition to caries; persistence of the milk-teeth, irregular implantation, and occasional absence of certain teeth. Dental dystrophies are more common in the second dentition, but may affect the first.

3. *Hare-lip and Cleft-palate.*—Kirmisson has noted the frequent coincidence of hare-lip with other signs of heredo-syphilis.

4. *Ocular Dystrophies.*—Partial union of the eyelids; coloboma of the eyelids and iris; abnormalities of the pupil; ophthalmoscopic rudimentary stigmata. The latter are rather the remains of syphilitic lesions of the fundus oculi than true dystrophies (*vide* Chapter XIX.).

5. *Auricular Dystrophies.*—Deformed shape of auricles, especially the satyr-shaped or ass's ear.

6. *Dystrophies of the Limbs.*—Asymmetry; elongation or stunting (both increase and diminution of growth may be caused by the influence of heredo-syphilis on the epiphyseal cartilages); polydactyly and syndactyly; ectromelus—a term applied to arrest in development of segments of a limb, including 'congenital amputations' (some of Barnum's armless and legless 'freaks' were cases of this kind); congenital dislocation of the hip; pelvic deformities; congenital club-foot. The last is attributed to intra-uterine poliomyelitis. Perrin mentions a case of four children with congenital club-foot, procreated by a syphilitic father.

7. *Cerebro-spinal Malformations.*—Meningocele, encephalocele. and spina bifida, absence of corpus callosum, micromyelia, porencephalia, anencephalus, etc.

8. *Cardiac and Vascular Dystrophies.*—Malformations of the heart, including absence of the right heart, persistent ductus arteriosus, patent foramen ovale, mitral stenosis; congenital cyanosis; Raynaud's disease and paroxysmal hæmoglobinuria; hæmophilia.

9. *Dystrophies of the Alimentary Canal.*—Imperforate anus, congenital hernia, œsophageal diverticulum, Meckel's diverticulum, etc.

10. *Genito-urinary Dystrophies.*—Ectopia vesicæ, epispadias, hypospadias, cryptorchidism; vulvar, vaginal, and uterine malformations.

11. *Cutaneous Dystrophies.*—Ichthyosis; some cases of alopecia areata; nævi; dermoid cysts; sclerodermia; prurigo of Hebra; and possibly other dermatoses of obscure etiology.

12. *Dystrophic Effects on the Nervous System.*—The nervous system is especially affected by heredo-parasyphilis, which may cause idiocy, imbecility and juvenile dementia, and is

probably one of the chief causes of insanity. Other manifestations of heredo-parasyphilis are juvenile tabes and general paralysis, congenital spastic paralysis and epilepsy (*vide* Chapters XII. and XVIII.).

13. *Fœtal Dystrophies.*—Arrested development of the amnion and hydramnios; monstrosities of all kinds. According to the observations of Edmund Fournier, heredo-syphilis appears to be the chief factor in teratology, and other factors, such as tuberculosis and alcoholism, which are often given as causes of monstrosity, are probably of secondary importance. Chronic alcoholism in the parents is a possible factor, but the transmission of tuberculosis, even in the form of 'paratuberculous heredity,' is open to question. It is true that the experiments of Gley and Charrin on animals have shown that other bacterial poisons may produce many deformities in the fœtus, but in the human subject the syphilitic factor in heredity predominates over all others. As Ballantyne remarks: 'We cannot regard the coexistence of anomalies of structure (and more especially of malformations) and a syphilitic parentage as accidental. In isolated cases the association may be a coincidence, but the coincidences are numerous enough to enable us to affirm a relation of cause and effect.'

There is great variation in both the nature and quality of the dystrophies, and all degrees in heredo-syphilitic subjects may occur, from handsome and well-formed beings to monstrosities.

The dystrophies may or may not be associated with manifestations of active syphilis, but in most cases subjects with dystrophic stigmata remain free from active lesions, and may contract acquired syphilis. Thus, we may see cases presenting Hutchinson's teeth with signs of ordinary acquired syphilis. This is due to the possibility of reinfection of heredo-syphilitics with the acquired disease, and constitutes what Tarnowsky called 'binary syphilis.'

Rickets and Heredo-Syphilis. — The relation of rickets to heredo-syphilis has been much discussed. Parrot regarded rickets as 'a mode of expression of heredo-syphilis towards

the second year of life,' and Kassowitz stated that 'nearly all children affected with heredo-syphilis become rachitic.'

Fournier thinks that Parrot went too far in regarding rickets as a syphilitic affection, and considers that although heredo-syphilis is a strong predisposing cause to rickets, the latter may occur in the absence of parental syphilis. More recently, however, Gaucher gives his opinion that 'heredo-syphilis alone produces rickets.'

In some families rickets and heredo-syphilis have been seen to alternate, some children being rickety and others syphilitic.

Contagiousness of Heredo-Syphilis.

It has been stated by Coutts and others that the contagiousness of heredo-syphilis has been much exaggerated, and that cases of acquired syphilis in infancy have been mistaken for the hereditary disease. This statement is based on the rarity of cases of contagion seen in the out-patient practice of the large children's hospitals. Coutts, from his experience at the Shadwell Children's Hospital, says: 'I have personally never known an instance where syphilis was contracted from an infant with the inherited complaint, and this in spite of many thousands of healthy children and adults having been exposed to infection from cases under my care.'

Such negative evidence is of little value compared with the positive evidence of the infection of wet-nurses by syphilitic sucklings collected some years ago by Fournier. On this subject he observes: 'The examples of syphilitic infection transmitted in this way from sucklings to wet-nurses are too numerous to mention, and I have myself observed more than eighty. We may therefore say without exaggeration that every healthy wet-nurse by suckling a syphilitic infant runs a great risk of contracting syphilis, and only rarely escapes.'

Again, we know now that the tissues of the heredo-syphilitic infant contain quantities of the *Spirochæta pallida*, and clinical evidence shows that all the lesions containing this organism are contagious. The experiments of Neisser have also shown that monkeys can be inoculated with syphilis from various

organs of heredo-syphilitics (lungs, liver, spleen, suprarenal capsules, testicles, ovaries, and *nasal mucus*).

Whether the contagiousness of heredo-syphilis has been exaggerated or not is a matter of little moment; the point is that heredo-syphilis is essentially contagious, and to belittle this fact is a dangerous doctrine.

Acquired Syphilis in Infancy.

Acquired syphilis in infancy is more common than is generally supposed, and it is possible that many cases are mistaken for the hereditary disease.

Infants may be contaminated by syphilitic wet-nurses; by playing with, or by using the same bottles, spoons, etc., as heredo-syphilitic infants; or by contagion from adults during the promiscuous and excessive fondling to which infants are subject. Contagion from lesions of the mother's genitals during passage of the fœtus at birth is not proved, and must be exceptional, for the fœtus (in cases where it has escaped hereditary infection) is protected by the vernix caseosa.

Acquired syphilis in infants is similar to that of the adult, but modified owing to the conditions of development and function of certain organs. The chancre is generally small, and often escapes notice, and the secondaries may also be benign, so that the symptoms are much less severe in the early stages than in the case of the hereditary disease.

Differential Diagnosis.—The chief points in which acquired syphilis differs from hereditary are—(1) the presence of the chancre; (2) the more healthy general appearance; (3) the absence of the following lesions which are peculiar to heredo-syphilis: natiform skull, epiphysitis, snuffles, bullous palmar and plantar syphilides, the syphilide in placards affecting the face and buttocks, etc.; (4) the contrast between the age of the child and the quality of the lesions. For example, a roseola eruption and mucous patches in a child of twelve must be recent and hence acquired. On the other hand, *tertiary lesions* are often impossible to diagnose, for a gumma of the

palate in a child of twelve may be due either to hereditary or acquired syphilis, and the lesions are identical.

Hutchinson's teeth are pathognomonic of hereditary syphilis, but interstitial keratitis and syphilitic deafness may occur in the acquired disease, although they are much more common in heredo-syphilis. Radiating scars about the mouth are presumptive evidence of heredo-syphilis.

Infantilism may be caused by acquired syphilis in infancy, and Fournier mentions several cases in which this occurred. In one case a child, who was infected by a syphilitic wet-nurse, had no teeth till the age of two; did not walk till the age of three; became small and infantile, with atrophied testicles, and finally developed cerebral syphilis.

To sum up, acquired syphilis in infants is generally easy to diagnose from early heredo-syphilis; but later on in life it is more difficult, and in cases of tertiary syphilis it is impossible to distinguish between the two forms of disease in the absence of pathognomonic signs, such as Hutchinson's teeth, natiform skull, etc. This is a matter of minor importance as regards treatment, as this is the same in both cases; but the diagnosis of acquired from hereditary syphilis in infancy is important from the *medico-legal* point of view, chiefly with regard to infection of infants by wet-nurses, and criminal assaults on children.

Treatment of Heredo-Syphilis.

The treatment of heredo-syphilis includes the prophylactic treatment of syphilitic heredity, as well as treatment of the disease itself in the child.

Prophylactic Treatment.—If a syphilitic man or woman proposes to enter into the matrimonial state, he or she should undergo a course of at least six months' mercurial treatment immediately before marriage, even in cases where an interval of four or five years has elapsed since the last manifestations of the disease. In cases where marriage has been premature it is advisable to continue treatment during the first year, and also to avoid pregnancy.

It is hardly necessary to state that this programme is seldom

carried out, even if it is recommended, which is not often. The majority of married couples neither know nor care anything about syphilis, and attribute any evil which may befall their unfortunate offspring to neglect on the part of the medical attendant or nurse. A child with epiphysitis, or some form of syphilitic paralysis or deformity, is usually said to have been 'dropped by the nurse' or 'injured at birth by the doctor.'

Treatment of Mother during Pregnancy.—It has been pointed out by Fournier that in the case of a woman pregnant by a syphilitic father mercurial treatment of the mother during pregnancy may in many cases lead to the birth of a healthy child. Hence, when the father has married prematurely, or has developed recurrent symptoms of syphilis after marriage, it is wise to treat the mother, even if she is not infected by the husband.

The practical difficulty which arises in such cases is the revelation of the husband's disease to the wife, if she has hitherto been kept in ignorance of it. It is difficult to treat the mother for long without her becoming enlightened as to the state of affairs. In such a dilemma the responsibility must be placed on the husband.

This *prophylactic treatment of paternal heredity*, in order to be successful, must be begun in the early months of pregnancy, and, according to Pinard, it has little chance after the fifth month. Small doses of mercury only should be given, as the dose is intended for the fœtus, and not for the mother. Fournier recommends $\frac{1}{8}$ grain of proto-iodide, or the same dose of gray powder may be given. Pinard recommends continuous treatment during the whole pregnancy, but Fournier prefers the intermittent method—twenty days' treatment and ten days' rest every month.

It stands to reason that the father should also be energetically treated; and, as we have seen before, treatment of the father alone will sometimes lead to the birth of a healthy child after a series of abortions. Pinard advises treatment of the father for six months before each procreation, and treatment of the mother during pregnancy—in both cases with biniodide.

Curative Treatment.—The offspring of syphilitic parents may be born apparently healthy, but develop late heredo-syphilis in after-years. It is also important to bear in mind that heredo-syphilis is sometimes exclusively visceral, and may be present without external signs. The prognosis in such cases should therefore be guarded, and the child should be kept under continuous observation whenever possible. Marasmus is suspicious of heredo-syphilis, and when it occurs in spite of proper feeding is an indication for antisyphilitic treatment.

The two best *methods of administering mercury* to the infant are (1) by inunction, (2) by gray powder. The latter is the most common plan, $\frac{1}{3}$ to $\frac{1}{2}$ grain of hydrargyrum cum creta being given three time a day in a little sugar-of-milk. As the child grows older the dose should be increased to 1 grain. Inunction may be carried out by placing $\frac{1}{2}$ drachm of mercurial ointment on the infant's binder, the movements of the child causing absorption of the mercury. Comby, who uses inunction as a routine method in infantile syphilis, rubs the ointment daily on to alternate parts of the body. Some Continental physicians recommend subcutaneous injections, but these are unnecessary, and difficult to carry out in infants.

With regard to the *duration of mercurial treatment* in heredo-syphilis, there is a too prevalent idea that the treatment should be symptomatic, and administered only during the presence of active symptoms. This is an erroneous doctrine, as Fournier stated long ago; but, like many other truths which he has pointed out from time to time, it has not received proper attention. 'Why,' he observes, 'should not a heredo-syphilitic infant be treated like an adult? Why, after having cured it of actual manifestations, should we not attempt to preserve it from future manifestations which we know only too well are almost certain eventualities? Has syphilis two ways of being cured, one for the adult at the price of prolonged treatment, the other for the child with treatment for a few weeks or months? Since it is demonstrated that syphilis in adults is almost always only cured slowly and progressively

under the influence of prolonged medication, a kind of chronic depuration requiring at least several years, does it not follow by analogy and common sense that treatment of the same kind is necessary and indispensable for the cure of syphilis in the infant ?'

In carrying out this prolonged treatment, extending over several years, it is necessary to watch the growth of the child, the gain in weight, the state of the digestive organs, etc., and to suspend mercurial treatment if there are any indications that it interferes with nutrition. However, it is well known that gray powder can be taken by infants for long periods in small doses without causing any harm. Some authors have said that mercury interferes with dentition, but they have very likely attributed to the effect of mercury what was really due to heredo-syphilis.

In any case mercurial treatment by gray powder should be continued for at least a year after all symptoms have disappeared, and further courses of mercury should be given during the tenth and twelfth years. This should be carried out by the intermittent method in both cases: in the infant, a month's treatment with intervals of a week; in the child, six weeks' treatment with intervals of a fortnight. The lesions of late heredo-syphilis require similar treatment to that for the acquired disease, and iodides are often useful in this stage.

Cod-liver oil is a useful auxiliary medication both in the case of early and late heredo-syphilis.

Suckling and Wet-Nurses.

Whatever may be the degree of contagiousness of hereditary syphilis, as compared with the acquired disease, the rule should be that *a child suspected of having congenital syphilis should on no account be suckled by a healthy wet-nurse.*

The difficulty lies in the fact that the child is often born with no signs of the disease, and apparently healthy. The signs of hereditary syphilis appear at a variable period after birth up to the third and fourth month, after which time they

are exceptional. According to Pinard, 70 per cent. occur in the first month, 20 per cent. in the second month, and 10 per cent. in the third and fourth months. Hence during the first three or four months an infant born of syphilitic parents cannot be guaranteed non-contagious.

The following rules should be observed in such cases:

1. Every infant with syphilitic lesions should be suckled by the mother; or, if this is impossible, by the bottle. Fournier recommends suckling by the goat or by a syphilitic wet-nurse, when either of these is obtainable.

2. In suspicious cases, where the infant is apparently healthy, but the parents syphilitic, the child should not be given to a wet-nurse till four months old, before which time it must be fed by one of the above methods.

The disadvantage of these precautions is, of course, the deprivation of a certain number of suspected infants of the advantages of suckling. This no doubt raises the mortality among weakly children, who derive more nourishment from the breast than from the bottle. But this evil is less than that of the contamination of wet-nurses by infants who turn out afterwards to be syphilitic.

Infected Wet-Nurses.—Another point to be considered is the converse of the above—viz., the suckling of healthy infants by syphilitic wet-nurses. A nurse may be infected by a syphilitic infant, and, after leaving this infant, may be passed as a healthy nurse while she is in the *incubation stage of syphilis*, and may infect the next child she suckles.

The following prophylactic measures are suggested by Pinard for the protection of both nurses and sucklings:

For the Protection of Nurses.—(1) Syphilitic parents should be treated before procreation and during pregnancy. (2) They should be warned that their children may be dangerous for every breast except the maternal one. (3) A law should be passed proclaiming that no infant should be given to a wet-nurse except with a medical certificate guaranteeing the nurse against all risk of contamination from that infant.

For the Protection of Sucklings.—(1) A wet-nurse, before proceeding to suckle another infant, should require a medical

certificate stating that the infant she has just suckled is free from any contagious symptoms. (2) Any wet-nurse not possessing such certificate should be legally debarred from suckling for two months.*

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CHAPTER XVII

SYSTEMATOLOGY OF HEREDO-SYPHILIS

Cutaneous Syphilides.

HOCHSINGER pointed out a few years ago that in the fœtus the glandular organs are especially affected by the syphilitic virus during their development, and that the internal glandular organs are affected before the skin, because the skin glands are not developed till later. In the skin the sweat glands are first attacked, and, as those of the palms and soles are the first to develop, this accounts for the early appearance of palmar and plantar syphilides. This view has been confirmed by the recent researches of Levaditi, who has found that the *Spirochæta pallida* has a special predilection for the glandular epithelium, and penetrates the protoplasm of the hepatic, renal, supra-renal, and sudoriparous gland cells.

Erythematous Syphilides.—A roseola, similar to that of acquired syphilis, rarely occurs in the hereditary disease. The usual erythematous syphilide takes the form of reddish-brown macules, which later on become yellowish. These appear during the first few weeks, and chiefly affect the buttocks and thighs, but may be scattered over the body and face generally. This syphilide is sometimes difficult to distinguish from intertrigo of the buttocks and thighs due to diarrhœa, etc., but the latter is usually limited to the region covered by the diaper, while the syphilide is of a darker colour, generally extends down the thighs, and is usually present elsewhere.

Papulo-squamous Syphilides. — These are common in hereditary syphilis, and form characteristic *placards*, formed by the coalescence of adjacent papules. These placards are dark red or ham colour, and form large desquamating patches,

especially affecting the palms and soles, the buttocks and scrotum, the forehead and eyebrows, and the parts around the mouth. When situated in the folds of flexion these syphilides become fissured and form *rhagades*. These occur especially round the mouth, where they form radiating fissures, often leaving scars when they heal, which are valuable signs in the retrospective diagnosis of heredo-syphilis (circumoral syphilides).

Bullous Syphilide.—This, the so-called 'syphilitic pemphigus,' affects chiefly the palms and soles, and is characteristic of heredo-syphilis. It often appears during intrauterine life, and signifies a severe and often fatal type of the disease. The bullæ are filled with sero-sanious or purulent fluid, and are situated on dark red macules. When they rupture they leave a raw, purple, sanious erosion, which may undergo ulceration. The bullæ often coalesce, giving rise to large excoriations. They may appear in one or in successive crops.

The researches of Levaditi have shown that the bullæ contain the *Spirochæta pallida*, which migrates from the papillæ of the dermis to the lower layers of the epidermis. The cells of the epidermis become vacuolated, and contain the spirochætes.

Diagnosis.—The bullous syphilide can be distinguished from *pemphigus neonatorum* by the above characteristics, and by almost always appearing before the seventh day. Pemphigus neonatorum is benign, and seldom appears before the end of the second week; the bullæ have clear contents, and develop chiefly on the neck and trunk, instead of the palms and soles.

Ulcerative Syphilides.—Parrot regarded *ecthyma* of the buttocks, lower limbs, and abdomen in infants, as syphilitic, but other authors regard it as a pyodermatitis due to local streptococcal infection. This lesion appears to be the final stage in what Jacquet describes as *simple polymorphous dermatitis of children* ('post-erosive syphiloide'), which is a simple dermatitis, varying in degree from simple erythema to papules, vesicles, and ulcerations, and usually associated with infantile diarrhœa. Hence, as Sabouraud remarks, 'syphilis should not be diagnosed at first sight in cases of lesions of the buttocks in infants. If syphilis really exists, the lesions will seldom be the first and never the only ones.'

Alopecia.—Thinning of the hair, eyebrows, and eyelashes often occurs in early heredo-syphilis, and bands of alopecia may be seen on the sides of the head and the occipital region.

Onychia. — The nails may be affected with onychia or perionychia. In the former condition the nails become dry, shrivelled, and transversely furrowed, and may be shed. In perionychia a suppurating ulceration forms round the nail and detaches it. According to Comby and others, these two conditions may be produced by nutritive disorders other than syphilis.

Gummatous Syphilides. — These occur in late heredo-syphilis, and have the same characters as those of acquired syphilis. They are rare in early heredo-syphilis. They have a predilection for the front of the leg and the face. On the leg they resemble varicose ulcers, for which they are often mistaken. On the face ulcerated gummata may destroy considerable parts of the nose and lip, and simulate lupus. They are sometimes serpiginous and phagedenic, and may cause considerable destruction.

Diagnosis. — The progress of heredo-syphilitic gummatous ulceration is slower than in acquired syphilis, but always more rapid than *lupus*. Syphilis makes as much progress in a month as lupus in a year.

In the pre-ulcerative stage of *lupus* the nodules are soft, and have the characteristic apple-jelly or barley-sugar appearance, while in syphilis they are hard and brownish-red. The diagnosis between ulcerative lupus and the ulcerative gummatous syphilide is shown in the following table :

Lupus.	Heredo-Syphilis.
Areola.—Red or purple.	Brown or ham coloured.
Crusts.—Soft, thin, and fragile.	Hard, thick, adherent, and often stratified.
Borders.—Flat, thin, soft, irregular, and undermined.	Sharply-cut circular or polycyclic, and adherent.
Base.—Shallow, pale red, sometimes with exuberant granulations (framboesiform).	Deep, irregular, and covered with a yellowish-gray slough of necrosed gummatous tissue.
Cicatrix. — Irregular, contractile, bridled, and bluish-red.	Regular, flat, at first brown, afterwards depigmented in centre, and finally white.

None of these signs are absolutely pathognomonic, and the diagnosis is sometimes only cleared up by the presence of other signs of heredo-syphilis (Hutchinson's teeth, signs of old keratitis, deformity of the nose, etc.), or by the effects of anti-syphilitic treatment, which should be tried in all doubtful cases.

Lupus generally affects the same place for years, while syphilis is more migratory. Fournier states that many cases of late heredo-syphilitic ulceration are diagnosed as lupus, and it is quite possible that some of the cases which fail to react to the Finsen and X-ray treatment may be cases of heredo-syphilis, and not lupus.

From *varicose ulcer* the syphilitic ulcer may be distinguished by the following signs: The syphilitic ulcers are usually situated on the front of the tibia; they are sometimes multiple, sometimes confluent; they are rounded or polycyclic from the confluence of several ulcers; their borders are sharply cut and surrounded by the copper-coloured areola which is characteristic. Sometimes these ulcers cicatrize spontaneously and partially, and a new ulceration may arise in the cicatrix; in fact, the characters are the same as those of gummatous ulcers of acquired syphilis. When ulcers agreeing with the above description are met with on the front of the leg, syphilis should be suspected, even if varices exist, for the existence of these varices constitutes an important predisposition to ulcers of the leg, whether specific or not, and in doubtful cases anti-syphilitic treatment should be tried.

Apart from the face and leg, the *genital region* requires special mention as an occasional localization of gummatous ulcerations. In women the labia, and in man the glans penis may be affected. In these regions the lesions sometimes simulate a soft chancre, or even a phagedenic chancre. Fournier mentions the case of a young virgin who was unjustly accused because she presented chancriform ulcerations, whereas she was the subject of heredo-syphilis, and was cured by specific treatment.

Syphilitic Lupus.—This term, which was applied by Hutchinson to cases of heredo-syphilitic ulceration which

simulate lupus, has been objected to, on nosological grounds, as causing confusion between tuberculous lupus and syphilis. As a matter of fact, the term is scientifically correct, and applies to those cases in which the tubercle bacillus is implanted on a heredo-syphilitic soil. It is now well known that syphilis predisposes to tuberculosis, and a combination (or symbiosis) of the tubercle bacillus and the spirochæte accounts for the hybrid lesions, the diagnosis of which is difficult to establish. This condition was recognised some time ago by Ricord, who gave it the name of *scrofulo-syphilis* (*scrofulate de vérole*); but after the discovery of the tubercle bacillus most lesions hitherto designated 'scrofulous' were banished from the domain of syphilis to that of tuberculosis. The discovery of the *Spirochæta pallida* may restore them to their proper place.

The Circulatory System.

Generalized *endo-periarteritis* in the fœtus was demonstrated by Bar and Tissier, and Levaditi has recently shown the prevalence of vascular lesions containing the *Spirochæta pallida* in heredo-syphilitic infants and fœtuses.

The Heart.—Cardiac lesions are found in syphilitic infants who die soon after birth. Microscopic gummata, interstitial myocarditis, and intracardiac hæmorrhages have been described. Mracek found intracardiac hæmorrhages due to endarteritis obliterans and thrombosis in 43 out of 132 syphilitic fœtuses.

Aneurisms have been reported in children, and also in the fœtus. Aneurism is liable to occur in the children of syphilitics at the age of twenty-five to thirty, and, according to Huchard, heredo-syphilis is a more common cause of aneurism than is generally supposed. 'Many cases of *aortitis* occurring in youth or adult age, aneurisms of the aorta and cerebral arteries developing without any apparent cause, as well as certain cardiac malformations (the so-called "pure" or congenital mitral stenosis), are the results of heredo-syphilis. This exerts its action on nearly all the organs, and it is truly

astonishing that authors have completely neglected the lesions of the circulatory apparatus' (Huchard).

According to Edmond Fournier, all *congenital malformations* of the heart (patent foramen ovale and ductus arteriosus, etc.) are stigmata of heredo-syphilis.

It therefore appears that heredo-syphilis may affect the whole of the vascular system in the same way as acquired syphilis, and that a generalized arterio-sclerosis of heredo-syphilitic origin, or *heredo-parasyphilitic arterio-sclerosis*, may result. It is obvious that this may explain many lesions of obscure etiology.

The Blood.—Syphilitic *anæmia* occurs in the hereditary as well as in the acquired disease. Gaucher describes the following forms: (1) Simple anæmia, with diminution of erythrocytes and hæmoglobin, and little or no increase of leucocytes; (2) *chlorosis*, with diminution of hæmoglobin out of proportion to the diminution of erythrocytes; (3) *pernicious anæmia*, with changes in form of the erythrocytes and diminution of hæmatoblasts; (4) *leukæmia* with nucleated erythrocytes, myelocytes, and hyperleucocytosis.

Paroxysmal Hæmoglobinuria. — Syphilis is now recognised as the chief cause of paroxysmal hæmoglobinuria, but its mode of action is obscure. The affection may occur in acquired or heredo syphilis, but is more common in the latter, either in infancy or in later years. It may accompany secondary and tertiary manifestations, or appear when syphilis is quiescent. According to Lépine, syphilis is a *sine quâ non* in the etiology of this affection, and malaria is of secondary importance. Cold is an exciting cause.

Pathogeny.—The essential change takes place in the blood, and the hæmoglobinuria is preceded by hæmolysis of the red corpuscles by some unknown agent in the serum (hæmoglobinæmia). Murri thinks the hæmolysis is due to changes in the hæmatopoietic organs caused by syphilis. The affection seems to be allied to Raynaud's disease, for during the paroxysms in severe cases vasomotor phenomena may occur, including cyanosis of the extremities and even gangrene of the nose, ears, and toes, acute cutaneous œdema, giant urticaria, and

purpura. In some cases the hæmoglobinuria alternates with Raynaud's disease, and Balzer suggests that they are both due to the same cause. Although the attacks are usually preceded by albuminuria, they do not appear to be due to any lesion of the kidney, for Dieulafoy and Widal found the kidneys normal, except for staining with extravasated hæmoglobin, in a woman who died during a paroxysm. According to Balzer, the evolution of the hæmoglobinuric paroxysm is probably as follows: Changes in the blood before the attack, depending on syphilitic infection; an exciting cause such as cold, which disturbs by reflex action the equilibrium by which the functions of the viscera may be carried on in spite of changes in the blood; congestion of the viscera, and especially the kidney, by this reflex; exaggeration of the changes in the blood; finally, accumulation of toxic substances which destroy the red corpuscles and give rise to hæmoglobinæmia.

Mercurial treatment is indicated in all cases of paroxysmal hæmoglobinuria, and under its influence the paroxysms often cease. Fournier, however, has recorded cases in which antisyphilitic treatment produced no effect, and some authors regard the affection as parasyphilitic.

The Spleen.— Hypertrophy of the spleen is common in early heredo-syphilis. Microscopic gummata have been described, but the usual condition seems to be one of vascular congestion with diffuse perivascular small-celled infiltration, which later on may undergo fibrous transformation. Levaditi has found endarteritis of the vessels, and numerous spirochætes immediately around them.

In late heredo-syphilis the spleen may be affected with tertiary lesions at the same time as the liver or kidney. Amyloid disease may also occur.

The Lymphatic Glands.—The subjects of heredo-syphilis are predisposed to enlargement of the lymphatic glands, and also to tuberculous infection of these glands. There may therefore be either simple hyperplasia, due to heredo-syphilis, or 'strumous glands,' caused by tuberculous infection of a syphilitic soil. Such cases should be treated with mercury before having recourse to operation.

The Alimentary System.

The Buccal Cavity.—In early heredo-syphilis *mucous patches* are common about the lips and inside the mouth, and constitute a source of infection for wet-nurses and others. Other children may be infected by using the same bottle or spoon, etc.

Mucous patches may be distinguished from *aphthous stomatitis* or thrush. Aphthous stomatitis commences in the form of minute pustules, which soon ulcerate, forming circular yellow ulcers with a bright red areola. The mucous patch is a flat grayish-red erosion. The aphthous ulcer is more painful than the mucous patch.

Tertiary Lesions. — In late *heredo-syphilis* gummatous lesions may affect the soft and hard palate in the same way as in acquired syphilis, and tertiary ulceration may attack the tongue, tonsils, fauces, and pharynx. Lesions of the pharynx often coexist with others affecting the nose, palate, or larynx.

As in the acquired disease, the chief diagnosis has to be made from lupus and tuberculous ulceration. *Lupus* is rare, and generally associated with lupus of the face, and differs from tertiary syphilis in the following points: (1) The stage of infiltration is much slower than in gumma; (2) the lesion consists of nodular hypertrophy with granular vegetations; (3) ulceration is slower and more circumscribed, and the ulcer is surrounded by pink granulations (apple-jelly nodules); (4) it is less extensive, more irregular, and less excavated; (5) lupus is often multiple, syphilis generally single; (6) lupus never perforates the centre of the palate like syphilis.

Fournier is of opinion 'that the sum total of lupus of the bucco-pharyngeal mucous membrane would be considerably diminished if a number of cases were subtracted by which it is illegitimately enriched at the expense of unrecognised heredo-syphilis.'

Tuberculous ulceration generally occurs with pulmonary tuberculosis, and is rarely primary. The tuberculous ulcer differs from the syphilitic as in the acquired disease (p. 132).

The Teeth.—Syphilis affects the teeth in two ways—(1) by retarded eruption; (2) by arrested development and malformation. Malformations consist in the so-called 'erosions,' microdontism, amorphism, abnormal implantation, and vulnerability, and are all due to the influence of syphilis on the dental system during its development. This influence may affect both dentitions, but is more common in the second, and of more importance in this case for retrospective diagnosis. The malformations are generally multiple and symmetrical.

DENTAL EROSIONS.—This term includes diverse malformations produced during the course of the intrafollicular life of the tooth, and resulting in a peculiar change in the crown, which appears worn and corroded—an apparent wear and tear of the teeth. But the term 'erosion' is not strictly correct, for this presupposes a healthy original, whereas the true condition is one of arrested development.

Hutchinson's Teeth.—The most characteristic erosions are those affecting the free borders of the incisor teeth. These may consist in (1) simple irregular notching; (2) an edge like a saw; (3) thinning of the free border; (4) general atrophy of the summit; (5) semilunar or crescentic notching or 'Hutchinson's teeth.' The typical Hutchinson's erosion consists in a marked crescentic notching of the free border, with bevelling of the anterior edge, rounding of the lateral angles, shortening of the vertical diameter, and convergence of the axis of the teeth. It is symmetrical, and generally affects the upper median incisors of the second dentition. It may occur in other incisors, and also in the first dentition. It may also affect only a single tooth.

This type differs in degree at different ages. The tooth does not emerge from the gum in its typical form, the notch being filled with small atrophic dental vegetations, the remains of atrophic changes during development. These become worn away in a few years, leaving the typical notch. The characteristic form is lost after adolescence, and at about twenty-five years the edge becomes horizontal by wearing away. After the thirtieth year 'Hutchinson's teeth' cease to be typical.

Other forms of dental erosions are—(1) *pitted erosions* forming small grayish-black dots, chiefly affecting the upper incisors; (2) *transverse furrows* of the incisors; (3) *atrophy of the cusp*, affecting the first molar and canine.

Different types of dental erosions may occur in the same subject; they may affect either dentition, but chiefly the second. In order of frequency they affect the first molar, the incisors, and the canines. The reason of this is that the ones affected are those which are undergoing dentification when hereditary syphilis is in an active state. This period corresponds to the first three or four months of life, when hereditary syphilis is at its maximum. The teeth in process of evolution at this period are the first large molars, which begin to dentify in the sixth month of fœtal life; the incisors in the first month of extra-uterine life, and the canines in the third or fourth month.

The erosions of homologous teeth occupy exactly the same level on the crown, but different levels on teeth of different orders. These differences of level are in anatomical relationship with the chronological differences in evolution of the different teeth.

The teeth in heredo-syphilis may also be affected by—(1) *microdontism*, usually affecting a few teeth only, and generally associated with other malformations; (2) *amorphism*, consisting in deviation from the normal type, so that canines resemble incisors and *vice versâ*; (3) *premature caries*; (4) *white transverse streaks*, usually affecting the upper median incisors; (5) *irregular implantation*.

Etiology of Dental Malformations. — Dental erosions were attributed by Magitot to infantile eclampsia, but their connection with hereditary syphilis was demonstrated by Hutchinson and Parrot. Moreover, infantile eclampsia is a frequent symptom of hereditary syphilis.

Dental erosions are said to occur in non-syphilitic subjects, and also in the cow, dog, and other animals. Hence syphilis would appear to be not the only cause.

Fournier concludes — (1) that the dental malformations known as erosions may arise from different causes; (2) that

syphilis appropriates these lesions more than any other pathological state; (3) that, as regards retrospective diagnosis of hereditary syphilis, the erosions have a very unequal value—some are nearly positive, others may be due to other causes; (4) that Hutchinson's teeth are almost a certain sign of hereditary syphilis; atrophy of the summit of the first molar and erosions in furrows are presumptive evidence of syphilis, but the pitted and other erosions are of less diagnostic value.

Parrot showed that a number of alleged causes of erosions, such as eruptive fevers, scrofula, and rickets, were negatived, because in most cases the teeth were already formed at the time when these affections occurred. Fournier, however, mentions that diseases which the mother may contract during pregnancy may affect the development of the teeth of the fœtus. The first molar begins to dentify in the sixth month of fœtal life, and hence may be affected during the last three months of pregnancy by disease of the mother.

Although it is possible that other diseases than syphilis may affect the fœtal dentition by attacking the mother during pregnancy, we must remember that syphilis is the one which most frequently occurs.

The Liver.—The liver is affected perhaps more than any other organ in heredo-syphilis, owing to the fact that it receives the maternal blood direct by the umbilical vein.

In heredo-syphilitic infants the liver is yellowish-gray in colour and hard ('flint liver'). On section small bodies are seen, resembling semolina grains. These are miliary syphilomata, and resemble miliary tubercles in appearance. In rare cases caseous gummata are seen. The histological changes consist in a diffuse small-celled infiltration between the liver cells, due to proliferation of pre-existing connective-tissue cells, and of the endothelium of the capillaries and lymphatics inside the hepatic lobules. The small cells become fibroblasts, and give rise to monocellular or pericellular cirrhosis. Later on there is fibrous-tissue formation with thickening of Glisson's capsule in the portal canals, and also accumulation of small round cells which form miliary syphilomata. This

process of pericellular cirrhosis closely resembles diffuse sarcoma, and is probably often mistaken for it. Along with these interstitial changes there is *endarteritis*, *endophlebitis* of the hepatic veins, and granular degeneration of the liver cells. Hepatic syphilis *in utero* may cause hydramnios from obstruction of the umbilical vein.

In *late hereditary syphilis* the hepatic lesions are tertiary in character, and resemble those of acquired syphilis. Perihepatitis is common, and *ascites* may occur either from perihepatitis or from pressure of enlarged glands in the portal fissure. Jaundice is rare. The liver and spleen are usually enlarged. Amyloid disease of the liver is common in late heredo-syphilis. Heredo-syphilis of the liver accompanied by ascites may be mistaken for *tuberculous peritonitis*, especially as the subjects are usually more or less cachectic and emaciated. In such cases the diagnosis depends on the presence of other signs of heredo-syphilis—signs of old keratitis and Hutchinson's teeth, etc. It is, however, advisable to try mercurial treatment in all such doubtful cases.

Levaditi has found the *Spirochæta pallida* in large numbers in cases of both early and late heredo-syphilis. The organisms were present both in the liver cells and in the walls of the hepatic veins.

Parasyphilitic Multilobular Cirrhosis.—Rolleston states that the pericellular cirrhosis of heredo-syphilis and early acquired syphilis differs too much from multilobular ('alcoholic') cirrhosis to be directly transformed into it. But pericellular cirrhosis leaves damaged tissues which are liable to be affected by multilobular cirrhosis under the influence of other causes, such as alcohol. Hence the term 'parasyphilitic multilobular cirrhosis' may be applied to these cases, and alcoholic or multilobular cirrhosis may be regarded as of parasyphilitic origin (see also p. 147).

The Pancreas.—The pancreas is affected more often in heredo-syphilis than in the acquired disease, usually in the form of interstitial fibrosis. Syphilitic pancreatitis is probably a cause of diabetes occurring in children and adolescents (see p. 217).

The Intestine.—Heredo-syphilitic affections of the stomach and intestines have not been much studied, but there is no reason why they should differ from those which occur in the acquired disease. Possibly some cases of round ulcer of the stomach and duodenum are due to heredo-syphilis or heredo-parasyphilis. Parrot described gummatous infiltration and ulceration of Peyer's patches.

The Respiratory System.

The Nose.—In early heredo-syphilis rhinitis (snuffles) is a characteristic symptom which usually occurs during the first three months. It is due to a swelling of the mucous membrane, with muco-purulent or sanious discharge from the nose, which dries and forms crusts, causing irritation and fissures of the upper lip. This condition may block the naso-pharynx, and seriously interfere with suckling and respiration. It may also spread to the Eustachian tubes and set up otitis media, or to the larynx, causing œdema and reflex spasm of the glottis, croup, or convulsions.

Gastou describes the following forms: (1) Anterior rhinitis, which only differs from simple coryza by its long duration and the occurrence of fissures and erosions about the nose. This form is generally benign. (2) Posterior rhinitis, which is accompanied by slight discharge, but causes troubles of respiration and deglutition. This form is readily curable by mercury. (3) Subacute adenoiditis, which is rarer than the above, and generally follows them. It begins with acute pharyngitis, and continues with symptoms of adenoid vegetations. It is often complicated by otitis, laryngitis, and broncho-pneumonia. It is cured with difficulty, and always leaves an inflammatory residue, which later on develops into adenoids. (4) Suffocating rhino-laryngitis, which is sometimes fatal soon after birth. The mucous membrane is dry and swollen, and its sensitiveness causes spasm of the glottis and sudden death. (5) Septic rhino-pharyngitis, which is usually a complication of the other forms. This may be the origin of infectious lesions affecting other organs. In the acute form there is a

fœtid sero-purulent discharge; in the subacute form laryngeal and pulmonary complications, which are often fatal; in the chronic form signs of septicæmia, with visceral lesions and cutaneous ulcerations.

Syphilitic rhinitis may lead to hypertrophic rhinitis, atrophic rhinitis, and ozæna, necrosis of bone, chronic laryngitis, ethmoiditis, retropharyngeal abscess, and adenoids. It may also lead to dystrophies and arrest of development. Local antiseptic treatment is required in addition to mercury.

Tertiary Lesions.—In *late heredo-syphilis* the lesions are similar to those of acquired syphilis. Gummatous infiltration may attack the muco-periosteum, and lead to subsequent necrosis of the vomer and nasal bones.

The alæ nasi and lower part of the septum may also be mutilated. Late heredo-syphilis of the nose is insidious in development, and painless. There are usually signs of coryza and nasal obstruction, with a sanious discharge from the nostrils. Sequestra of bone may continue to be discharged for months or years, constituting one form of *ozæna*.

Nasal Deformities. — Falling in of the root of the nose is due to necrosis of the nasal bones, and this deformity is a 'certificate of syphilis, acquired or hereditary.' Falling in of the lower part of the nose is due to loss of the septum, resulting in more or less invagination of the lower segment on the upper. This deformity is named by French authors the *nez en lorgnette*, or telescoped nose.

Perforation of the palate is generally due to gummatous osteitis extending from the nasal cavities to the mouth. It is usually near the middle line, and the occurrence of perforation is revealed by the sudden change in the voice and the reflux of liquids through the nose.

Diagnosis.—The chief points of difference between the heredo-syphilitic gummatous ulceration of the nose and *lupus* are as follows: (1) Lupus rarely attacks the bone, and is usually confined to the soft parts and cartilage, while syphilis may extend to the nasal bones, ethmoid, sphenoid, vomer, turbinals, and palate. (2) Lupus is generally symmetrical, syphilis asymmetrical. (3) Lupus is more typical after cicatrization

than when active, leaving thin white parchmenty cicatrices, and when extensive a 'death's-head' deformity of the nose with a truncated nasal stump and open cavity.

The Larynx.—Laryngitis is common in early heredo-syphilis at the same time as snuffles. A hoarse aphonic cry in an infant is suggestive of heredo-syphilis. Syphilitic infants are liable to (1) *sudden spasm of the glottis*, associated with snuffles, which may be fatal; (2) symptoms of *croup*, caused by ulceration of the mucous membrane of the larynx. This form usually occurs after the third month, and may be mistaken for diphtheria.

In *late heredo-syphilis* the larynx may be affected by the remains of lesions dating from infancy, or from fresh lesions. Syphilitic laryngitis occurring in infancy may leave cicatrices, stenosis, and fibroid induration of the mucous membrane, and these tissues are liable to break down during an attack of measles, whooping-cough, or typhoid. Sir Felix Semon reported two cases of heredo-syphilitic infants who were affected with syphilitic laryngitis in the first month: one died of dyspnœa at the age of five, caused by chronic thickening of the glottis; the other died at the age of three from acute œdema of the glottis.

Tertiary Laryngitis occurs in late heredo-syphilis in the same forms as in the acquired disease, and may take the form of circumscribed gummata, ulceration, or more often sclero-gummatous infiltration ending in sclerosis. Tertiary laryngitis often coexists with gummatous ulceration of the throat. It has to be *diagnosed* from lupus and tubercle.

Lupus is rare, and almost always secondary to lupus of the throat or skin, much slower in evolution, nearly always limited to the epiglottis, and of a granular purple appearance.

Tuberculous laryngitis is almost always preceded by pulmonary tuberculosis, and presents the general symptoms of tubercle. It is of slower evolution than syphilitic laryngitis. The presence of the tubercle bacillus will assist the diagnosis. According to Krishaber, 'the colour and extent of the lesions is almost completely without value in establishing a differential diagnosis between syphilitic and tuberculous laryngitis.'

The Lung.—In *early heredo-syphilis* a form of broncho-pneumonia occurs which was formerly called the 'white pneumonia of Virchow.' This consists in a diffuse interstitial pneumonia, chiefly peribronchial in localization, and accompanied by endo-periarteritis and catarrhal desquamation of the bronchial tubes and pulmonary alveoli. It differs from other forms of broncho-pneumonia in the predominance of the interstitial and vascular changes over the catarrhal. It may end in resolution or may undergo caseous degeneration, constituting 'white hepatization,' which is a common cause of death in heredo-syphilitic infants. In other cases it leads to chronic pulmonary fibrosis with dilated bronchi. Levaditi describes infiltration of the perivascular tissue with mononuclear cells, and filling of the alveoli with large mononuclear and polynuclear cells. Spirochætes were present in great numbers along the walls of the capillaries and in the alveoli, the latter being phagocyted by the large mononuclear cells filling the alveoli.

In *late heredo-syphilis* the pulmonary lesions resemble those of the acquired disease, and consist of gummata and interstitial fibrosis. It is probable that many cases of heredo-syphilitic pneumonia are attributed to tubercle; but it must always be remembered that heredo-syphilis is a predisposing cause to pulmonary tuberculosis (see p. 168). Therefore heredo-syphilis should always be borne in mind in the case of a child or adolescent with signs of phthisis.

The Genito-urinary System.

The Kidneys.—The kidneys may be affected in both early and late heredo-syphilis. Cassel has found interstitial infiltration of the kidney and cystic degeneration of the glomeruli in syphilitic fœtuses. Massalongo reported a case of renal syphilis in an infant of eight months, with other specific lesions; endo-periarteritis was found in the renal vessels, as well as in the liver and spleen; histologically, the changes in the kidney were those of interstitial nephritis.

Leonard Guthrie has reported several cases of chronic interstitial nephritis in children, some of which died of cerebral

hæmorrhage, others of uræmia. The kidneys were in a condition of diffuse interstitial nephritis, with endarteritis. The nephritis was attributed to heredo-syphilis.

Coupland has also reported two cases of nephritis in the subjects of heredo-syphilis. In the first, a girl of thirteen, there were evident signs of hereditary syphilis and renal dropsy; at the autopsy the kidneys were found affected with parenchymatous nephritis, and there were gummata in the liver. In the second case, a girl of eighteen, there were periosteal nodes in the legs and necrosis of the frontal bone; death was caused by nephritis, and the kidneys were affected with parenchymatous changes; gummata were found in the bones and liver.

Levaditi has recently demonstrated the presence of the *Spirochæta pallida* within the cells of the epithelium of the convoluted tubules in heredo-syphilitic infants.

The Suprarenal Glands.—These are frequently affected in heredo-syphilis, either by miliary gummata or sclerosis. Levaditi has found the *Spirochæta pallida* in considerable numbers, both intra- and extra-cellular. It is possible that heredo-syphilis of the suprarenals may account for some cases of Addison's disease.

Another point of interest is the possible relation of syphilitic disease of the suprarenal glands to *arterio-sclerosis*. Josué has produced atheroma in rabbits by injection of adrenalin into the veins, and it is conceivable that disease of the suprarenal glands might cause arterio-sclerosis by discharging into the circulation products of disordered metabolism. In this way a general parasyphilitic arterio-sclerosis might be produced, distinct from atheroma caused by endarteritis of the vasa vasorum (see Chapter VI.).

The Ductless Glands.—The apparent predilection of the *Spirochæta pallida* for the glandular organs, including the ductless glands (suprarenals, spleen, and thymus), suggests the possibility that disorders of the internal secretion of these glands may be caused by syphilis, and that the dystrophic effects of heredo-syphilis may be largely due to disorders of internal secretion caused by morbid changes in the ductless glands by the *Spirochæta pallida*.

It is also conceivable that *myxœdema* and *acromegaly* may owe their origin to disordered internal secretion caused by the effects of heredo-syphilis on the *thyroid gland* and *pituitary body* respectively.

The Testicles.—Heredo-syphilis may affect the testicles in two ways—(1) by arrest of development, usually associated with infantilism; (2) by interstitial orchitis. In the first condition the testicles are small, rudimentary, and usually functionless; in the second they are uniformly enlarged, hard, and painless. Orchitis is usually bilateral, and when occurring in an infant is diagnostic of heredo-syphilis. This condition may cause atrophy of the testicles and consequent sterility. Later on the relics of the atrophied testicles are felt as hard nodules, the size of a nut or olive.

The Ovaries.—Syphilis of the ovaries has not been investigated to the same extent as syphilis of the testicles, but these organs are probably sometimes affected with the same process of interstitial sclerosis. When affecting both ovaries this process will lead to sterility, and this is possibly one reason why cases of transmission to the third generation are not more frequently met with.

The Uterus.—Heredo-syphilis is probably the chief cause of malformations of the uterus (uterus septus, bicornis, and didelphys, elongation of cervix, anteflexion, etc.), as of other congenital deformities due to arrested development.

The Osseous System.

The parts of the osseous system which are in active growth during the last few months of fœtal and the first few months of extra-uterine life are especially attacked by the syphilitic virus.

Hochsinger distinguishes the following varieties of bone lesions in early heredo-syphilis:

1. Disorders in growth and inflammatory changes in the region of the epiphyseal cartilages.
2. Hyperplastic periosteal inflammation.

3. Periosteal and endosteal rarefaction.

4. The formation of abnormal medullary spaces in the cartilage and bone.

5. Excessive calcification of the epiphyseal cartilages.

6. Diffuse cell proliferation in the endosteal medullary spaces.

7. Degenerative lesions in the medulla.

8. Necrosis in the zones of proliferation, and calcification of cartilage.

Osteochondritis or Epiphysitis.—This generally occurs in the first few months, and affects the knees, elbows, wrists, and ankles. The process, which may begin in intra-uterine life, consists in vascular changes at the junction of the diaphysis with the epiphysis, resulting in irregular proliferation and fatty degeneration of the cartilage, with imperfect ossification. Suppuration may occur, causing separation of the epiphysis. On section of the bone an irregular yellow zone is seen, representing the degenerated epiphyseal cartilage.

Pseudo-Paralysis.—The immobility of the limb caused by epiphysitis was named by Parrot *syphilitic pseudo-paralysis*. Although epiphysitis is perhaps the most common cause of paresis of the limbs occurring in infants, Hochsinger is of opinion that some cases are due to *myositis* without bone affections, and others to changes in the central nervous system.

According to Hochsinger, *heredo-syphilitic myositis* originates from periostitis at the points of insertion of the muscles. The rare condition known as *myositis ossificans* may possibly be explained in this way. Hochsinger also describes *tetany* in newly-born syphilitic infants, and attributes it to the action of toxins on the central nervous system. The so-called *sterno-mastoid tumour* of infants is better attributed to syphilitic myositis than to 'injury during birth.'

Dactylitis.—This is a form of osteochondritis affecting the phalanges. According to Hochsinger, syphilitic dactylitis usually affects the first phalanx only; never the second and third without the first; it is characterized by a painless swelling confined to the phalanges, without implication of the joints; sometimes bilateral, generally multiple, and tending to spon-

taneous resolution without suppuration. It usually occurs in infancy, but Hochsinger has seen ten cases between the ages of one and five years. Tuberculous dactylitis differs from syphilitic in affecting the distal phalanges and in the tendency to suppuration, caries, and implication of the soft parts.

Gaucher, however, states that the signs of syphilitic dactylitis are sometimes indistinguishable from tuberculous.

Parrot's Nodes.—This name is given to a symmetrical form of osteoperiostitis affecting the frontal and parietal bones in infancy, and leaving nodes which constitute a characteristic 'hot-cross-bun' deformity, or natiform skull. Parrot regarded this affection as exclusively heredo-syphilitic, but others have attributed it to rickets. The probability is that Parrot's nodes are always due to heredo-syphilis, but as the latter is a predisposing cause of rickets, they are often found in rickety children. It is very doubtful if rickets by itself can give rise to this condition.

Craniotabes.—This is a condition of thinning of parts of the skull, chiefly affecting the occipital bone and the region of the lambdoid suture. It is due to the effect of pressure on imperfectly developed bone. Craniotabes was formerly regarded as a sign of rickets, but Barlow pointed out its association with heredo-syphilis, and stated that this condition was seldom seen in rickets unless associated with congenital syphilis. The probable explanation of both Parrot's nodes and craniotabes is that they are heredo-syphilitic phenomena occurring in a rickety infant.

Tertiary Lesions.—In late heredo-syphilis various forms of osteoperiostitis and osteomyelitis occur, which are often confounded with 'tubercle.'

There is still a tendency to regard nearly all bone disease in children as tuberculous, whereas many cases are syphilitic either in nature or in origin, and it is probable that not a few cases which are submitted to various forms of operative procedures would clear up under antisyphilitic treatment. In other cases the heredo-syphilitic soil is vulnerable to the attacks of the tubercle bacilli, and in this way a hybrid lesion is produced, vaguely known as 'strumous' or 'scrofulous.' In

1886 Fournier wrote: 'Everything which in a child or adolescent affects a bone, with the sole exception of traumatism, is *ipso facto* attributed to scrofula.' This is almost equally true at the present day, substituting 'tubercle' for 'scrofula.'

Gaucher relates several cases of chronic bone disease with fistulæ, which were diagnosed as tuberculous and repeatedly scraped, but which soon healed under antisyphilitic treatment.

Osteoperiostitis.—This affects the long bones chiefly, also the bones of the skull. The tibia is most often affected, and after this the ulna, radius, humerus, femur, clavicle, and fibula. The lesions are generally multiple, often symmetrical, and generally localized to the diaphysis. The affected bone is increased in size and changed in form. In the case of the tibia the well-known and characteristic 'sabre-blade' deformity with pseudo-rachitic incurvation is produced in this way. The enlargement of the bone is preceded by pains in the bone with nocturnal exacerbations, which is often attributed to rheumatism or 'growing pains.'

In some cases the osteoperiostitis undergoes suppuration and *necrosis*, and this may account for some cases of so-called 'acute necrosis.'

Gummatous Osteoperiostitis.—This is more rare, and consists in a localized gummatous infiltration of the periosteum, with caseation and subjacent osteitis. There is generally a peripheral zone of hardened bone with osteophytic outgrowths. The tibia and bones of the skull are most often affected by this form of osteitis, and in neglected cases necrosis takes place.

Osteoperiostitis may determine local muscular atrophy or arrest of development, and may also give rise to spontaneous fractures.

Diagnosis.—The chief points in the diagnosis of heredo-syphilitic osteo-periostitis are—(1) the predilection for the long bones; (2) the multiple and symmetrical lesions; (3) the slow and chronic evolution, leading to hyperostosis; (4) the changes in form of the affected bone; (5) the osteocopic pains with nocturnal exacerbations which often precede the visible lesion.

Exostoses of growth are distinguished from syphilitic osteo-

periostitis, by being limited to the junction of the diaphysis with the epiphysis, and by being painless and of slower growth. The simple exostosis is a circumscribed nodule, while the syphilitic exostosis is a general swelling of a segment of the bone.

Tuberculous bone disease is distinguished from syphilitic osteo-periostitis by the following points:

1. It has a predilection for short bones such as the tarsus, vertebræ, and epiphyses; also the malar bone, ribs, sternum, scapula, and pelvis; while syphilis affects chiefly the long bones.

2. The tuberculous process is one of rarefying osteitis or caries, while the syphilitic process is one of osteoperiostitis with hyperostosis and sometimes necrosis. Bazin remarks that 'caries is a termination of tubercle, while necrosis is a lesion of syphilitic nature.' Bazin also found syphilis in the parents of children affected with spontaneous necrosis.

3. The pains in tubercle are vague and dull; in syphilis they are often severe, and characterized by nocturnal exacerbations.

4. In tubercle the evolution of the lesion is slower, there is less bony growth, and the soft parts are thickened and infiltrated.

5. Suppuration is more common in tuberculous than in syphilitic bone disease, but not so rare in the latter as is generally supposed (Gaucher).

6. The general health is more affected in tubercle than in heredo-syphilis, and there are often signs of pulmonary or glandular tuberculosis.

Cranial Deformities.—The chief cranial deformities caused by heredo-syphilis are—(1) the nasal deformities caused by destruction of the nasal bones and vomer (saddle-back nose and *nez en lorgnette*); (2) the natiform skull, caused by Parrot's nodes in infancy, in which the top of the skull is square and the frontal eminences prominent; (3) general prominence of the forehead, with increase in both height and width, called by French authors the 'Olympian forehead'; (4) asymmetry of the skull; (5) microcephalus and hydrocephalus; (6) high

arching of the palate bones (*palais ogival* of the French). This last is by some authors attributed to faulty development caused by the presence of adenoids in infancy; but, according to Gastou, syphilitic coryza in infants may lead to the growth of adenoids (p. 360).

Malformation of the jaw is a common result of heredo-syphilis. The most common form is *prognathism* of the lower jaw, preventing complete inclusion of the lower teeth within the upper, and causing prominence of the chin. Another malformation sometimes seen is deficient vertical development of the *premaxillary bone*, owing to which the incisor teeth do not meet when the mouth is closed. This defect is often accompanied by incomplete development of the nose, and gives rise to a characteristic crescent-shaped profile.

Pelvic Deformities.—Heredo-syphilis may cause arrested development or malformations of the pelvis. Pinard has found various pelvic deformities in heredo-syphilitic subjects, including the flat or 'rickety' type, and narrowing of the transverse or oblique diameters from unilateral or bilateral hyperostosis. It is probable that the so-called 'rickety' pelvis is caused more by heredo-syphilis than by rickets. It is also not impossible that *osteomalacia* may be a heredo-syphilitic phenomenon.

Osteitis Deformans.—Fournier regards osteitis deformans as a manifestation of late hereditary syphilis. Failure of specific treatment is no argument against this view, as the disease may be parasyphilitic. Osteitis deformans resembles certain forms of heredo-syphilis in the following points: (1) A predilection for certain long bones, especially the tibia; (2) multiple lesions, as a rule; (3) a premonitory painful stage; (4) massive hyperostosis; (5) the sabre-blade deformity of the tibia.

Gaucher has reported a case of osteitis deformans in a man of forty-eight which was improved by antisyphilitic treatment. The disease was of five years' duration, and affected the cranium, clavicles, femurs, tibias, and cervical vertebræ. After three months' treatment, with daily injections of 2 centigrammes of benzoate of mercury and 2 grammes

of iodide internally, there was considerable improvement in locomotion.

Arthropathies.—The joint affections in late heredo-syphilis include (1) arthralgia, (2) hydrarthrosis, (3) arthritis deformans.

ARTHRALGIA may be mistaken for rheumatism, but is distinguished by the nocturnal exacerbations of pain and by yielding readily to iodides.

HYDRARTHROSIS.—This is a chronic effusion chiefly affecting the knees, and is often symmetrical. It occurs during childhood, and is often associated with interstitial keratitis. According to Clutton, hydrarthrosis occurs independently of any bone lesion, but Fournier thinks there is usually epiphyseal periostitis near the synovial membrane, which can only be found by careful examination.

OSTEOARTHRITIS.—In some cases there is 'syphilitic white swelling,' caused by hyperostosis of the epiphyses, with slight effusion and thickening of the perisynovial tissue. This is probably often mistaken for early *tuberculous disease* of the joint, but differs in the following points: (1) Absence of pain and immobility; (2) absence of suppuration; (3) the skin is unaltered; (4) there is only slight limitation of movement, and the patient can walk; (5) absence of wasting and hectic fever. This form of syphilitic joint disease is most common in the knee, but sometimes affects the elbow and ankle.

ARTHRITIS DEFORMANS.—There sometimes occurs in heredo-syphilitic children a form of chronic arthritis of the smaller and larger joints characterized by osteophytic outgrowths from the epiphyses, which cause limitation in movement of the affected joints and a certain degree of muscular wasting. In some cases there is said to be ankylosis. These cases usually occur between the ages of five and twelve, and are often associated with interstitial keratitis or choroiditis, which also occur at this period.

Syphilitic arthritis deformans must be distinguished from a form of chronic joint disease in children described by Still. This affection, which occurs before the second dentition, is characterized by elastic fusiform enlargement of the joints

without bony change, by enlargement of the spleen and lymphatic glands, and by the frequent presence of adherent pleura and pericardium. It affects chiefly the knees, wrists, spine, ankles, elbows, and, later on, the fingers; in severe cases most of the joints may be affected. It differs from syphilitic arthritis in the absence of changes in the bone.

Although Still's joint disease differs essentially in its clinical features and morbid anatomy from heredo-syphilitic joint disease, it is quite possible that it may be of *parasyphilitic* origin. A point in favour of this view is the general arrest of development which has been noted when the disease occurs before the second dentition.

As Fournier remarks, 'Given in a child or adolescent an arthropathy which is not categorically explained by any evident morbid influence, accidental or constitutional, hereditary syphilis should always be borne in mind as a possible cause of this arthropathy.'

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CHAPTER XVIII

HEREDO-SYPHILIS OF THE NERVOUS SYSTEM

AFFECTIONS of the nervous system in hereditary syphilis may be roughly divided into (1) lesions of evolution and development; (2) syphilitic lesions proper. But there is no absolute line of demarcation.

Lesions of Evolution and Development.

These cause the formation of monstrosities, and may be considered to include almost the whole of teratology; but how far the nervous system acts in these cases it is difficult to determine. Congenital talipes has been attributed to poliomyelitis of syphilitic origin, and the children of syphilitics often suffer from congenital deformities. Ingelrans mentions an interesting case of a child with an atrophied forearm, whose father had syphilitic hemiplegia and symptoms of cerebral syphilis at the time when the child was conceived.

Hydrocephalus.—The connection between hydrocephalus and syphilis is based on the frequency of its occurrence among infants born of syphilitic parents, and on the frequency of abortions in the mothers of hydrocephalic children. Hochsinger found 35 cases of hydrocephalus in 362 cases of early heredo-syphilis. In 15 cases it began from the third to the eleventh month; in 6 it was intra-uterine. Several of these subjects had normal intelligence at two or three years of age, but 24 showed cerebral manifestations, including persistent vomiting, retraction of the neck, convulsions, contractures of the limbs, idiocy, nystagmus, and spasm of the glottis. Of these 24 cases, 16 were cured of the symptoms, 3 improved, and 5 died with other signs of syphilis. Hochsinger regards some

cases of hydrocephalus as due to rickets. This involves the question of the relation of rickets to heredo-syphilis, which is discussed on p. 338.

The essential morbid change in hydrocephalus consists in degeneration of the optic thalami, so that the ventricles form a single cavity. This is explained by the tendency of syphilis to attack organs in process of development, and in the infant the basal ganglia are in a state of great activity. Most cases of hydrocephalus die in convulsions in the course of a few months or years, but a few reach adult age, with more or less impairment of intelligence.

Intellectual Decadence.—Hereditary syphilis may cause arrest of intellectual development, varying in degree from deficient intelligence to idiocy. The development of the brain may be retarded in several ways: by thickening of the bones of the skull due to syphilitic osteitis; by chronic meningitis; by sclerosis with atresia of the cerebral arteries. The last is probably the most common origin of atrophy of the brain in hereditary syphilis.

The clinical picture is well drawn by Fournier: 'In a first degree we have subjects poor in spirit, unintelligent, simple, silly, dull. As children, they are of slow development, both physically and morally. They cut their teeth later; they remain for a long time small, puny, and stunted. They also begin to talk late. Later on they have great difficulty in learning to read and write. Their vocabulary is always very restricted and their memory defective. At the age of ten or twelve years their amusements and games are those of children of a younger age. At the age of adolescence they become bad scholars, making little progress, and always behind their fellow-students—stupid, dense, simple, obtuse, and silly; in fact, incapable of true intellectual culture. They are politely called "backward children."'

In a second degree they are 'beings destitute of all intelligence, incapable of any rational psychic manifestation, incapable even of attention. Not only are they rebellious to all attempts at instruction, education, and moral culture, but they hardly understand what is said to them, or sometimes do not under-

stand at all. They do not speak, or have only at their disposal a few elementary words, which they seem to articulate with difficulty, and which most often they mutter. If their life is not absolutely limited to eating, drinking, and sleeping, it is restricted to a series of instinctive actions without conscious motive—to coming and going without purpose, to infantile occupations, to inapt amusements, to foolishness of all kinds, even to machinations which renders them sometimes dangerous, to say nothing of a variety of transient incidents, such as unreasonable anger, cries, violence, sudden and brutal impulses, alternate attacks of excitement and depression, etc. Also it is not uncommon to observe, coincidently with this degradation of the intellectual and moral faculties, certain sensory disorders (dimness of vision or amblyopia); or, more often, transitory or permanent disorders of motion, such as uncertainty and clumsiness of movements, awkwardness of the hands, trembling, weakness of the limbs, staggering, want of equilibrium, etc.'

Idiocy.—The investigations of Edmond Fournier tend to show that hereditary syphilis is the chief cause of developmental defects and malformations, including those of the brain; and Solovtzoff attributes all congenital malformations of the nervous system to heredo-syphilis. Therefore, as the great majority of idiots are caused by defective cerebral development, it would appear that hereditary syphilis must be regarded as the principal cause of idiocy.

On the other hand, statistics compiled by Fletcher Beach and others only show a percentage of hereditary syphilis in 1 to 2 per cent. of idiots. This apparent contradiction is probably explained by the difficulty in obtaining a history of syphilis in the parents, and by the fact that the classical signs of hereditary syphilis are frequently absent in the subjects of syphilitic heredity. It must be remembered that it is only recently that general paralysis has been recognised as of syphilitic origin, and this only after the most careful investigations, conducted by many observers. If the same amount of care was taken to study the antecedents of idiots, it is probable that a syphilitic ancestry would be found in most cases.

It is difficult to accept a percentage of only 1 or 2 per cent. of hereditary syphilis in idiots, as this must be considerably lower than the percentage in other children.

Professor Fournier states that 'it is more common for the influence of hereditary syphilis to manifest itself by a more marked degeneration of the intellectual faculties—a degeneration ending in or confined to *idiocy*.'

Judson Bury, on the other hand, writes that congenital deficiency of mind from heredo-syphilis is probably rarer than mental failure coming on in childhood; and Fletcher Beach considers that heredo-syphilis tends to cause *juvenile dementia* rather than idiocy. In any case, the essential point to realize is, as Bury remarks, that 'hereditary syphilis is a more frequent factor in the production of mental disturbance than has hitherto been recognised.'

Such cases would be still more common if it were not for the fact that lesions which are capable of such an effect on the intellectual faculties are frequently fatal.

Syphilitic Lesions Proper.

The morbid changes met with in heredo-syphilis of the nervous system are identical with those of the acquired disease, and consist in vascular and meningeal inflammations and gummatous formations. Cerebral hæmorrhage, and softening secondary to thrombosis are less common than in acquired syphilis. The most common lesion is basal meningitis.

Some attribute all cases of chronic encephalitis in infants to heredo-syphilis; others to the results of acute infectious diseases, alcoholism in the parents, lead and mercury poisoning, and 'paratuberculous heredity.' It would appear to be more rational to attribute them to well-known and common causes, such as hereditary syphilis and chronic alcoholism in the parents, than to paratuberculous heredity, which is open to scepticism.

Symptomatology.

Hereditary syphilis reproduces most of the chief symptoms which occur in acquired cerebral syphilis—viz., headache,

vertigo, convulsions, partial or general epilepsy, partial paralysis, ocular paralysis, hemiplegia, sensory disorders, intellectual changes, coma, etc.

Secondly, hereditary cerebral syphilis proceeds, like acquired cerebral syphilis, by initial forms which are essentially multiple and varied, to end later on in a group of symptoms which are more characteristic. In other words, it is *polymorphous at its commencement and more uniform when more advanced.*

In one case it begins with headache; in another with epileptic attacks; in a third with mental disorder; in a fourth with ocular paralysis, and so on. As it advances it gradually tends to assume less multiple and diverse clinical forms, finally ending in a syndrome of identical symptoms, characterized chiefly by motor paralysis and intellectual disorders, in the form of hebetude, depression, and destruction of the mental faculties.

The three chief characteristics of hereditary cerebral syphilis at its onset are (1) headache, (2) epileptic attacks, (3) disordered intellect. These three forms of onset may be considered separately.

Type with Initial Epileptic Symptoms.—The epileptic attacks of cerebral syphilis are generally preceded for some days or weeks by severe headaches with nocturnal exacerbations, transitory attacks of vertigo, or mental dulness. The attacks themselves are 'identical with those which occur in essential epilepsy.' They have the usual symptoms of sudden onset, preceded or not by an aura; followed by loss of consciousness, tonic convulsions of short duration, clonic spasms of longer duration, foaming at the mouth, biting the tongue, stertor, and sleep; awakening with no recollection of the attack, and after this mental hebetude—in fact, all the symptoms of *grand mal.* Forms of *petit mal* sometimes occur, but are more rare. They consist in partial convulsions of the facial muscles, transient loss of consciousness, or falling without loss of consciousness.

The epileptic symptoms may continue without other cerebral signs, or the initial epilepsy may become effaced by more complex cerebral phenomena. Cases of the first class resemble

those of essential epilepsy. Ripoll has reported a case in which epileptic symptoms lasted for ten years in a boy of twelve, the son of a syphilitic father. Periostitis then developed, and under specific treatment both the epilepsy and the periostitis were cured.

The second class of case, in which the epileptic attacks gradually diminish and are replaced by other cerebral symptoms, is more common. These cerebral symptoms may consist in (1) congestive attacks, of headache, giddiness, tinnitus, or amblyopia; (2) moral changes, in character and temper, causing apathy or irritability; (3) intellectual changes, leading to mental dulness, loss of memory, and progressive diminution in intelligence; (4) paralytic phenomena, including partial paresis or paralysis, especially affecting the ocular muscles, and finally hemiplegia, which is the usual termination.

The course of heredo-cerebral syphilis is thus the same as in cerebral acquired syphilis, in which the epileptic form often begins as a pure epilepsy, and continues in this form for a time, to be afterwards effaced progressively in relative importance by the addition of other symptoms, finally ending in cerebral disorganization.

Fournier describes the case of a little girl, the child of syphilitic parents. The first child was stillborn; the second child died in six weeks with syphilitic lesions; the third child, the one in question, showed signs of hereditary syphilis at the age of three weeks, but developed into an apparently healthy child till the age of nine years.

'At this time she began from time to time to urinate in bed at night. She was scolded, but without any effect on this symptom, which is often a sign of unrecognised nocturnal epilepsy. Some time after this she was suddenly attacked with convulsions while at dinner. She lost consciousness suddenly, and became as stiff as a bar of iron; she had general convulsions, foamed at the mouth, bit her tongue, passed urine involuntarily, etc. Similar attacks followed at irregular intervals, and always with the same symptoms. The child was regarded as epileptic, and submitted to a series of divers medications which had no effect. Five or six months passed without any other phenomena, except some change in character and a certain degree of intellectual weakness. Then, while the epileptic attacks continued, the scene was changed. Intelligence rapidly declined

memory was lost. The child forgot what she had learnt—history, geography, catechism, etc. She only understood with difficulty. She sometimes had strange and extraordinary ideas. At other times she was frightened without cause, and burst into fits of stupid and prolonged laughter, etc. She became undocile, mischievous, peevish, irritable, and morose. A little later speech became embarrassed, certain words were badly pronounced, scanned or 'mangled.' Sensory troubles appeared: vision became weak; the pupils dilated widely, but unequally in both eyes; hearing was diminished; sensation was retarded, so that when a limb was pinched the pain was only noticed after several seconds. From time to time attacks of vomiting occurred. Motion was then affected, and muscular power decreased. The movements became feeble and undecided; walking was staggering and uncertain; objects were let fall by the hands, etc. Sometimes there were intermittent contractions of certain groups of muscles, especially those of the jaw; jerking of the limbs, etc. Paralysis of the sixth nerve on the left side, with strabismus and diplopia, occurred; also involuntary micturition and defæcation. In the course of a few months all these phenomena underwent progressive increase in spite of intense specific treatment (which, as a matter of fact, was given too late, at a time when the situation was already almost desperate). Intelligence was completely lost, and the child was transformed into a veritable idiot. Sight was lost; all the limbs were affected by paresis; the hands could no longer hold anything; the lower limbs were unable to support the body; mastication was difficult and slow; deglutition was so imperfect that solids could be scarcely swallowed, and liquids were partly rejected by the nose. For several weeks life was no more than automatic, vegetative. Finally hemiplegia developed with coma, which in a few days ended this lamentable scene. An autopsy was made, and revealed undoubtedly specific bony lesions; thickening of the meninges; meningo-cerebral adhesions; disorganization of the gray matter, and foci of softening in the central regions. This is an example of hereditary cerebral syphilis with initial manifestations of an epileptic nature.'

Type with Initial Cephalalgia.—Headache is rarely absent among the initial symptoms, but varies much in intensity and duration. It is sometimes slight and ephemeral, but more often intense and continuous. It may continue for some time as the only symptom, or may be from the first associated with other cerebral phenomena. As in the headache of acquired syphilis, it is characterized by its *nocturnal exacerbations* and its *persistence*. It persists for days or weeks, with or without intermissions, affecting the whole head rather than

any particular point. A headache of this kind is by itself strongly suggestive of cerebral syphilis.

Under treatment by mercury or iodide the headache is rapidly relieved, and gradually disappears; but when left to itself it is generally complicated by other symptoms, such as disorders of intelligence, epileptic attacks, paresis or paralysis, to end finally in a complex and severe cerebral condition. These complications usually follow the headache more quickly in heredo-syphilis than in the acquired syphilis of adults. However, in rare cases the headache may persist for a long time without further symptoms. Augagneur relates the case of a heredo-syphilitic man aged twenty-six who suffered from constant headache with nocturnal exacerbations, together with periostitis of the tibias. For five years he was treated for rheumatism with salicylate of soda, etc. He was eventually rescued by Augagneur, and treated with iodide of potassium, with the result that both the headache and the alleged 'rheumatism' disappeared.

Hence the syphilitic headache, with the above-mentioned characteristics, is the chief premonitory symptom of cerebral syphilis, and is an indication for prompt and energetic anti-syphilitic treatment.

Type with Initial Mental Symptoms. — In most cases this coexists with other cerebral phenomena of various kinds; but sometimes it may for a time predominate or exist as the only symptom. This type is constituted by both mental and moral disorders, and comes into the category of cases which are popularly described as 'brain fever.' Fournier mentions the case of a child who, after being cured of lesions of hereditary syphilis in infancy, developed cerebral symptoms at the age of nine, and died in fifteen months. The first symptoms consisted exclusively of intellectual and moral changes, which later on were complicated by epilepsy; the child's affection for relatives and friends was lost; by degrees she became indifferent, harsh, peevish, cross, sulky, and extremely irritable; she passed from gay to sad without reason, and sometimes wept for hours without apparent cause.

Such is the commencement of the type with initial mental

symptoms. As a rule, this is soon followed by other signs, the chief of which are headache, congestive attacks of vertigo, amblyopia, etc., and epilepsy. These symptoms generally appear in a few weeks, and end in a complex cerebral condition. This type with initial mental symptoms has the worst prognosis, and is the most rebellious to treatment of all the different forms of hereditary cerebral syphilis.

In some cases, however, this type, which is usually only a prelude to more complex and severe cerebral manifestations, may persist in a permanent mental form, at any rate for a considerable time. This constitutes the type known as the 'backward child,' with retarded mental and physical development. Such cases may become imbeciles. Hughlings Jackson relates the case of a young man, born of syphilitic parents, who lost all intelligence at the age of fifteen years, and without any other cerebral phenomena.

The three types described above constitute the most usual initial manifestations of cerebral heredo-syphilis. There may be, however, other morbid phenomena at the onset of the disease, either isolated or associated with the preceding.

These are—(1) *congestive disorders*, comprising vertigo, giddiness, tinnitus, and sometimes sudden disturbance of equilibrium; (2) *paralysis of the ocular nerves*, especially the third nerve, often partial (ptosis or mydriasis) and generally unilateral, as in the adult; (3) *hemiplegia* may occasionally occur as an early sign, but more commonly at a later period.

Later Manifestations.—After the initial manifestations the pathological field becomes enlarged and the affection becomes more general, diffuse and multiple in its morbid expressions, ending in a complex totality with numerous and diverse symptoms. For instance, a case commencing with headache as the predominant symptom may be followed by various congestive disorders, epileptic attacks, disordered intelligence, sensory affections, motor disorders, convulsions, paralyses, coma, etc.

There are numerous varieties of the ulterior symptoms, depending on the situation, extent, and number of the cerebral lesions. In spite of the diversity of these symptoms, there are

certain fundamental phenomena which, although varying in degree and in date of appearance, are found in all cases. These are *intellectual and motor disorders*. The intellect is always affected in the advanced stages of the disease. Intellectual disorders may occur among the first symptoms, and, after progressive increase, end in absolute dementia.

Motor disorders are common, and occur in variable forms: ocular paralyses, causing strabismus, ptosis, mydriasis, etc.; paresis or partial paralysis, affecting half the face, one limb, the tongue, pharynx, sphincters, or bladder; or a peculiar state of general paralysis affecting all the limbs, especially the lower limbs; or hemiplegia. Hemiplegia may be absolute, or more often partial, and constitutes the usual termination of the disease.

In addition to the mental and motor changes, which constitute the fundamental symptoms of the disease, there are (1) epileptic attacks, which are usually prolonged to an advanced period, and may constitute the ultimate stage in which the patient succumbs; (2) disorders of sensation, including diminution of general sensation, deafness, and amblyopia; (3) transient attacks of aphasia, muscular spasms, convulsions, and contractures.

Donkin records cases with one-sided convulsions and hemiplegia in children, and one case of aphasia in a child four years old.

Prognosis.—Untreated cases, after arriving at the advanced stage, usually end fatally at a variable period, which may occur rapidly or slowly. An example of slow evolution is given by Judson Bury, which lasted for eight and a half years, presenting the following symptoms: At the age of three years epileptic convulsions with right paresis; at the age of four and a half years the child could not walk; at the age of nine there was progressive aphasia; soon after this the child became a complete idiot, and finally died at the age of eleven and a half with epileptic attacks. At the autopsy there was found thickening of the cranial bones considerably reducing the left middle cranial fossa; diffuse meningitis; atrophy of the left temporo-sphenoidal lobe; arterial sclerosis, etc.

Diagnosis.—Hereditary cerebral syphilis has to be diagnosed from *tuberculous meningitis*, *cerebral tumour*, and '*essential epilepsy*.'

Tuberculous Meningitis.—This resembles cerebral syphilis in the prodromal symptoms of mental asthenia and headache, and in the later symptoms of physical weakness, restlessness, insomnia, partial or general convulsions, localized paralyses (especially ocular), paralysis of the third nerve (ptosis, strabismus, mydriasis), monoplegia and hemiplegia.

Cerebral syphilis differs from tuberculous meningitis in the usual absence of the following points, which are characteristic of the latter disease: (1) Fever, (2) retracted abdomen, (3) irregular pulse. In tuberculous meningitis the pulse is at first accelerated, but afterwards slow and irregular, and one of the chief characteristics of this disease is the slow pulse associated with fever. This syndrome is usually absent in cerebral syphilis. Other symptoms which are more marked in tuberculous meningitis are—obstinate constipation, vomiting, delirium, photophobia, contractures, grinding the teeth, and retraction of the head.

In doubtful cases diagnosis may be assisted by lumbar puncture. In both tuberculous and syphilitic meningitis there is lymphocytosis of the cerebro-spinal fluid, but the diagnosis may be settled by finding the tubercle bacillus, or by experimental inoculation of the guinea-pig with cerebro-spinal fluid.

Cerebral Tumour.—A cerebral gumma may cause the same symptoms as any other cerebral tumour, such as a tuberculous focus. In both cases the symptoms consist in headache, epileptic attacks, partial paralyses, etc., and the diagnosis can only be made indirectly by consideration of the general condition of the patient and his antecedents.

Epilepsy.—The type of cerebral syphilis with epileptic onset may simulate what is known as 'essential epilepsy' (p. 258). The chief points of distinction are the following: (1) Syphilitic epilepsy is symptomatic and connected by a common origin with other cerebral symptoms, such as headache, and disorders of sensation, motion, and intelligence—symptoms

which do not belong to 'essential epilepsy,' at any rate in its initial stages. It is not uncommon for hemiplegia to follow the epileptic attacks of cerebral syphilis, an event which does not occur in 'essential epilepsy.' (2) The number of epileptic attacks is more numerous in cerebral syphilis. (3) In syphilitic epilepsy there are other cerebral symptoms between the attacks, and the patient is not normal during these intervals, as in 'essential epilepsy.' (4) Syphilitic epilepsy is frequently partial or unilateral.

Although it is of great importance to distinguish syphilitic from 'essential' epilepsy, this does not affect the question of the parasyphilitic origin of 'essential epilepsy,' which is discussed on p. 256.

The Spinal Cord.

The study of hereditary syphilis of the spinal cord, apart from spinal paralysis caused by gummatous hyperostosis of the vertebræ ('syphilitic Pott's disease'), is of recent date, and is due chiefly to the work of Gilles de la Tourette in 1896. The following year Gasne showed that a number of heredo-syphilitic fœtuses and stillbirths presented spinal lesions which would have caused clinical symptoms if they had not died from the effects of syphilis *in utero*.

Marfan has recently observed a general process of endarteritis and endophlebitis affecting the arteries and veins of small and medium calibre, ending in thrombosis and foci of hæmato-myelia. Sometimes isolated areas of sclerosis occur apart from the meninges.

Clinically, the lesions of the cord are manifested by paralysis, which is generally slow in evolution, and accompanied by shooting pains in the limbs. If the upper cervical region is attacked, there may be quadriplegia, and also signs of bulbar paralysis. Sensory disorders and sphincter troubles occur, according to the localization of the lesion. Extension to the bulb and base of the brain may cause vertigo, ptosis, diplopia, gastric crises, and dyspnœa. If the dorso-lumbar region is affected extensively, it gives rise to the classic form of syphilitic meningo-myelitis, with symptoms of spasmodic

paraplegia, exaggerated reflexes, ankle clonus, and sphincter troubles.

In nearly every case the disease takes a progressive course. The arms and legs are at first affected with paresis, which proceeds to paralysis, more often spasmodic than atrophic, and often accompanied by pain or anæsthesia. The anæsthesia and paralysis may be crossed, forming the type of Brown-Séquard's paralysis. The tendon reflexes are generally exaggerated and seldom absent. The chief characteristic of heredo-spinal syphilis is the extreme diffusion of the lesions, but they are more common in the cervical and dorsal than in the lumbar region. The intensity of the symptoms is relatively slight when compared with the extensive region attacked, this being shown by the preservation of certain spinal functions, while others are destroyed. Another characteristic sign is the early disappearance of some symptoms and the persistence of others. Diagnosis is often aided by the appearance of cerebral and ocular symptoms. Rapid improvement under treatment, and relapses are common (Sachs).

Hereditary syphilis may attack the spinal cord at three periods of existence—(1) in intra-uterine life; (2) from infancy to adolescence; (3) from adolescence to adult age. Hence the lesions may be congenital, early, or late.

Congenital Hereditary Syphilis.—This includes cases of stilibirths and infants which die soon after birth. The pathological process is often generalized, affecting both the brain and spinal cord, and also the viscera. The meninges and bloodvessels are chiefly affected, and the spinal cord is invaded by the syphilitic process, affecting the pia mater and its intraspinal prolongations, especially along the vessels. The whole process consists, therefore, of an embryonic meningo-myelitis of vascular origin, analogous to the diffuse interstitial hepatitis met with in the same cases, and is essentially of the same nature as the meningo-myelitis of acquired syphilis.

If the child is born alive, there are clinical symptoms due to sclerosis, which is a more advanced stage of the embryonic process of meningo-myelitis. These symptoms are almost

invariably both cerebral and spinal, owing to the disseminated nature of the lesion, but in some cases the spinal symptoms predominate.

Congenital Spastic Paraplegia. — This clinical type is known in France as Little's disease; in England as congenital spastic paraplegia. The disease was described as congenital spastic rigidity in 1861 by W. J. Little, who attributed it to some abnormal change in the circulation during parturition, causing asphyxia. The symptoms consist in rigidity and slow movements of the lower limbs, causing walking to be delayed till four or five years of age. The toes drag on the ground, the thighs are adducted and rotated inwards, and the feet are in the position of equinus. This gives rise to 'cross-legged progression.' The legs are stiff and rigid, the arms less so, and the reflexes are exaggerated. The condition is one more of contracture than paralysis; sensation is normal, and the intellect is not affected, although there may be some affection of speech. The lesion is said to be due to retarded development of the pyramidal tracts.

That syphilis was a factor in the etiology of this affection was pointed out by Fournier and Gilles de la Tourette, who reported two cases procreated by syphilitic fathers. In one there were signs of heredo-syphilis, and both cases improved under antisyphilitic treatment. Dejerine has described syphilitic changes in the bloodvessels. Vizioli reported the case of four sisters, with a syphilitic father, all of whom presented spasmodic rigidity of the limbs, with difficulty in speech and deglutition, and also signs of heredo-syphilis affecting the teeth and skull.

The heredo-syphilitic origin of this disease thus appears to be well established, and shows, by the absence of cerebral symptoms, such as epilepsy, nystagmus, or strabismus, that congenital heredo-syphilis may in some cases almost exclusively affect the spinal cord, giving rise to a form of spastic paraplegia resembling in most respects that of acquired syphilis. The differences would appear to be due to the fact that in the congenital form the child is affected before it has learnt to walk.

The investigations of Charrin and Léri are interesting in connection with congenital heredo-syphilis. These observers have found microscopic hæmorrhages in the nervous system of stillborn infants in cases of infective diseases of the mother. If these infants had survived, the hæmorrhagic foci would have destroyed the nerve tissue or opposed its development, thus creating congenital cerebro-spinal defects. These lesions may explain certain arrests of development and the formation of cavities, as in syringomyelia. In the case of heredo-syphilis the hæmorrhages would be consecutive to syphilitic vascular lesions, and due to the softness of the tissues of the fœtus.

Early and Late Hereditary Syphilis.—In the congenital cases the pathological changes consist in a process of embryonic infiltration, ending in sclerosis if life is sufficiently prolonged. As the subject advances in age, the tissues become more and more differentiated, and the spinal cord, meninges, and vessels may each be affected on their own account. The embryonic infiltration collects in gummatous deposits, which may be interstitial, meningeal, or perivascular. Arteritis, arterio- and phlebo-sclerosis are produced, and the clinical field is enlarged. Owing to the initial generalization of the pathological process there is a tendency for both brain and cord to be simultaneously affected. Hereditary syphilis of the cord does not differ essentially from acquired syphilis; acute and chronic myelitis may occur, also bulbo-spinal forms, and others exclusively medullary.

The difficulty lies in establishing the connection of the paralysis with heredo-syphilis rather than in diagnosing the seat of the lesion. In early cases occurring during childhood the spinal manifestations are rarely isolated, and other signs of hereditary syphilis can usually be found, such as keratitis, dental and other dystrophic stigmata. Cases occurring in adolescence are difficult to distinguish from acquired syphilis, in the absence of definite heredo-syphilitic stigmata. Hereditary syphilis of the spinal cord is even more subject to recurrences than acquired syphilis.

Bulbo-spinal Paralysis.—This is well illustrated by a case of late hereditary syphilis reported by Raymond. A male,

aged twenty, was hydrocephalic from birth, and suffered from severe headache and vertigo at the age of thirteen. After an interval of five years the following symptoms were noticed: Pain in the neck and shoulders, nocturnal headache, and inclination of the head to the right. This was followed by rapid muscular atrophy of the thenar, hypothenar, and forearm muscles; knee-jerk absent on the right side and weak on the left; slight anæsthesia on the left side; hearing and taste diminished on the left side; pupils unequal, but reacted to light and accommodation; white atrophy of the papilla; nystagmus; partial paralysis of third and sixth cranial nerves, and incoordination in the dark. The sphincters were normal.

The diagnosis was probably basal meningitis with cervical pachymeningitis. The painful torticollis, pain in the shoulder, and atrophy of the muscles of the hand, were due to pachymeningitis implicating the seventh and eighth cervical and first dorsal nerves. Motor inco-ordination in the lower limbs was due to leptomeningitis of the left posterior column in the lumbar region of the cord. The affections of the eye and eye muscles were due to basal meningitis.

This case differed from Friedreich's disease in the presence of papillary atrophy and in the absence of affection of speech. Also, Friedreich's disease always begins in the lower limbs. It differed from multiple sclerosis in the presence of the nocturnal headache, and from cerebral tumour by the absence of vomiting and the five years' remission of headache. Syphilis is the only disease which will account for the above symptoms, and in the case in question improvement occurred under antisyphilitic treatment.

Chorea.—Cases of chorea have been observed in heredosyphilitic subjects, suggesting that syphilis may be one factor in the etiology of chorea. Allison reported four cases of chorea in children of syphilitic parentage, without any history of scarlet fever or fright, etc. In three cases the movements were unilateral and in one general, and in two cases there were preceding attacks of hemiplegia. Three of these cases were cured by mercury and iodides, and one died. Kowalesky observed a family in which all the children had chorea, and

the father was syphilitic. Nonne quotes a case of Zambaco's which resisted treatment by the usual remedies, but was cured by antisyphilitic treatment.

Hysteria and Neurasthenia.—Heredo-syphilis is probably a factor in the causation of both hysteria and neurasthenia, but these affections are better regarded as due to heredo-parasyphilis. *Enuresis* and *stammering* have also been attributed to heredo-syphilis by some authors.

As Ingelrans well remarks, 'heredo-syphilis of the nervous system is often unsuspected, although syphilis takes a large share in the etiology of nervous disease. When the etiology of a disease of the cerebro-spinal system is obscure, even if syphilis or heredo-syphilis appears improbable, it must nevertheless always be thought of. The frequency of heredo-syphilitic affections is not known. Everything depends on the clinical instruction of the observers, and also on the tendency that some have to think that too much is attributed to syphilis. Acquired syphilis in the infant must also be borne in mind. The therapeutic test often gives astonishing results.'

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SACHS AND SOLOVTZOFF (quoted by Ingelrans).

CHAPTER XIX

HEREDO-SYPHILIS OF THE EYE AND EAR

HEREDITARY syphilis may affect the eye in intra-uterine life, in infancy, at puberty, or in adult age. The distinction between the early and late manifestations of hereditary syphilis is somewhat artificial, but useful clinically.

Early Hereditary Syphilis.

Iritis and Irido-cyclitis.—Hutchinson was the first to show that iritis constitutes a manifestation of hereditary syphilis, as well as of the acquired disease. In 1863 he reported twenty-three cases in subjects varying from six to eight weeks of age. Iritis may exist during intra-uterine life, but is rarely seen in the newly born. It generally occurs during the first few months, and is usually unilateral. Occasionally it occurs in late hereditary syphilis, between the ages of twelve and twenty years.

The clinical appearance is the same as in the iritis of acquired syphilis (p. 266), but it shows less reactional phenomena. It may be complicated by interstitial keratitis, in which we have seen that the uveal tract is usually affected. It has the same tendency as acquired iritis to form abundant plastic exudation and posterior synechiæ. The treatment is the same as for acquired iritis, but the prognosis is more serious.

The Choroid and Retina.—Choroiditis is generally intra-uterine, and leaves cicatricial lesions visible by the ophthalmoscope. These lesions may be divided into four types; but owing to the variations which the normal fundus may present

in different subjects, these dystrophic changes must not be mistaken for physiological varieties. On the other hand, Antonelli maintains that many of the ocular stigmata of heredo-syphilis have been wrongly described as varieties of the normal fundus.

1. The first type is characterized by a number of small reddish-yellow spots, more abundant at the periphery of the fundus. The papilla is normal or slightly atrophic, and there may be slight contraction of the field of vision. The affection is generally bilateral, but in mild cases the prognosis is favourable, because the lesion has little tendency to progress.

2. In the second type there occur pigmented foci, isolated or confluent, also yellowish-red spots, less abundant than the pigmented ones. These lesions are situated chiefly at the periphery, but may extend towards the papilla. Visual acuity is normal, but the field of vision is contracted at the periphery at the points corresponding to the retino-choroidal changes. The affection is usually bilateral, and may often be observed after resolution of interstitial keratitis.

3. The third type consists in the appearance of yellowish-white masses, with a tendency to fuse together. The retinal pigment has disappeared in the region of the patches, and is accumulated at their borders. These lesions are more marked at the periphery, but may extend to the posterior pole of the eye, and cause disorders of vision and marked contraction of the visual field. Prognosis is less favourable than in the preceding types.

4. The fourth type is more severe, with more extensive lesions and greater diminution in the visual field and in visual acuity. The pigment disappears in some places and accumulates in others, especially round the papilla. These pigmentary masses take diverse shapes, and are mingled with yellow foci of choroido-retinitis. The papilla is pale, but rarely ends in optic atrophy. The region included between the papilla and the pigmentary lesions has a gray or slate-coloured appearance, resembling the fundus oculi of a negro. The affection is nearly always bilateral, and often preceded by interstitial keratitis.

These are the four types which the lesions of hereditary syphilis may present in the choroid and retina, but they are not always so clearly differentiated, and may occur in mixed forms. Prognosis of the lesion itself is favourable in the milder forms, as it has no tendency to increase, and even in the severer forms intense visual disorders are nearly always due to other concomitant lesions.

Retinitis Pigmentosa.—This affection, which is always bilateral, is characterized by a progressive sclerosis of the retina, extending from the periphery to the centre. It manifests itself by small pigmentary masses, resembling bone corpuscles in shape, which are at first limited to the periphery and slowly invade the central parts of the retina, and finally cause atrophy of the optic nerves. The functional symptoms are at first slight, and characterized only by hemeralopia or night-blindness; but the visual field becomes gradually contracted, and the affection ends in blindness, which may not be complete till the fortieth or fiftieth year.

Apart from the special gravity of pigmentary retinitis, the objective signs which distinguish it from the preceding types are not always clearly marked. It may thus be described as another type connected with hereditary syphilis. At any rate the affection dates from intra-uterine life, and syphilis must be admitted as one of the possible causes, if not the only cause. 'The disease is often congenital, and frequently accompanied by other congenital defects, both of the eye and other organs. Deaf-mutes appear particularly liable to have retinitis pigmentosa' (Juler). The disease consists in atrophy of the nerve elements and the development of connective tissue. The walls of the vessels undergo hyaline thickening, and the fine arterioles are transformed into tracts of connective tissue. It is often found in members of the same family, and has been traced through several generations. All this evidence points to the syphilitic origin of retinitis pigmentosa.

Optic Neuritis.—Changes in the papilla are usually the result of preceding lesions. Primary optic neuritis is more rare in hereditary syphilis than in the acquired disease. Probably most cases of optic atrophy are the result of

pigmentary degeneration of the retina, and are not preceded by a neuritis.

Vascular Changes.—Changes in the retinal vessels give important evidence of former intra-uterine inflammation, which may be of syphilitic origin. The arteries are sometimes contracted, and the veins dilated and tortuous. It is not rare to see a segment of a vessel obliterated and transformed into a fibrous cord in consequence of endo- and peri-arteritis. Sometimes on each side of the vessel a white streak is seen, due to sclerosis of the walls of the vessel.

Congenital Malformations.—All congenital malformations of the eye (coloboma, microphthalmia, infantile glaucoma, congenital cataract) may be caused by hereditary syphilis (Edmund Fournier). Nystagmus and strabismus have also been attributed to congenital defects in the eye, of the same origin.

Strabismus.—In the opinion of Gaucher 'nearly all cases of strabismus are of specific origin.' Antonelli explains this by the occurrence of different degrees of heredo-syphilitic choroido-retinal stigmata in the two eyes, causing difficulty in binocular vision. Antonelli also states that arrest of development or malformation of the eye may cause *hypermetropia* associated with a certain degree of *astigmatism*. In these cases vision remains usually below normal, in spite of correction by glasses.

Myopia.—Lapersonne states that heredo-syphilis is the chief cause of rapidly developing *myopia* in young subjects, and advises that in every case of myopia the treatment should not be confined to the prescribing of glasses, but that the patient should be examined for signs of heredo-syphilis, and treatment instituted accordingly. He also remarks that if an adult myopic contracts syphilis, the treatment should be energetic, and the myopia and associated astigmatism should be carefully corrected.

The chief lesions found in cases of rapid myopia (malignant myopia) are those of choroido-retinitis. Interstitial keratitis may also give rise to myopia.

According to Antonelli unilateral *myopia* may be of heredo-

syphilitic origin, owing to the choroido-retinal stigmata being more advanced in one eye than the other, so that elongation of the axis of the eye is greater on the one side.

Late Hereditary Syphilis.

Interstitial Keratitis.—This has also been named 'parenchymatous,' in order to distinguish it from the superficial forms of keratitis. It begins insidiously with dimness of vision, without pain or general reaction. On examination of the eye by oblique illumination a number of gray points are seen on an opalescent base, occupying the substance of the cornea, giving the appearance of glass which has been breathed upon. The next stage consists in the development of absolute opacity of the cornea and the intervention of reactional inflammation. Owing to the opacity of the cornea the iris and pupil are obscured or completely invisible. A vascular ring appears round the cornea, formed by vessels arising from the anterior ciliary arteries. This vascular infiltration gradually extends to the tissue of the cornea, producing various tints according to degree. The first tint resembles that of salmon (the so-called 'salmon patch'); later on it becomes red, finally resembling an effusion of blood, which is due to a dense network of capillaries. At this stage the cornea is sometimes slightly eroded on the surface. The visual troubles vary from dimness to complete loss of vision. Photophobia, epiphora, and ocular pains vary in degree, but are less marked than in other forms of keratitis.

The third stage consists in resolution with progressive atrophy and disappearance of the vessels. The infiltration, especially under treatment, may become entirely absorbed, leaving the cornea as clear as before; but this is rare, and there is generally some cloudiness left. Sometimes, however, the infiltration persists and becomes organized in patches of sclerosis, generally situated in the centre of the cornea and interfering with vision. These patches are of importance for retrospective diagnosis, and consist of two kinds—(1) *leucoma*, an absolutely opaque white patch; (2) *nephelion*, or simple

gray translucent cloudiness. The latter may be situated centrally or peripherally, and is often only distinguishable by means of oblique illumination with a lens.

Interstitial keratitis usually affects both eyes, but seldom attacks both at the same time. However, both corneas may be opaque at one period. The disease is of slow evolution and long duration, the first stage lasting two or three weeks, and the second and third stages several months. The whole duration may thus be from six to eighteen months.

Complications.—The chief complication of interstitial keratitis is *irido-choroiditis*, and, according to some authors, the infiltration of the cornea is the consequence of changes in the uveal tract. This point of view is in accordance with facts, because syphilis attacks the uveal tract by preference, and choroiditis would probably be more often noticed if the corneal opacity did not hinder ophthalmoscopic examination.

Peripheral choroiditis, which is sometimes met with before or after interstitial keratitis, is also in favour of this view. *Iritis* or *irido-cyclitis* may occur at the onset of the affection, or after a few weeks, and the prognosis is always grave, owing to the liability to posterior synechia, opacities of the lens, or anterior capsular cataract.

The intra-ocular tension in interstitial keratitis is usually diminished; but sometimes it is increased, and staphyloma may occur several years after the disappearance of the corneal infiltration.

Prognosis.—This is grave, owing to the possible remains of the affection causing disturbance of vision, but chiefly because of the possible results of the irido-choroiditis which may accompany it. The results of treatment are usually successful, but not always, and some cases are rebellious in spite of energetic treatment. Recurrence is not common, but relapses are frequent, and may continue for years.

Etiology.—Interstitial keratitis is most common between the eighth and fifteenth years, but it is said to occur in the first few months of life, or even *in utero*. With regard to its syphilitic origin, Hutchinson in the last edition of 'Syphilis' (1899, p. 75) says: 'Interstitial keratitis, in its typical form, is

always a consequence of syphilis, and is in itself sufficient for the diagnosis.'

Opinions differ as to whether interstitial keratitis is exclusively caused by hereditary syphilis, or whether it may also occur in the acquired disease. Hutchinson says it is rare in acquired syphilis. Terrien says he has seen three cases in acquired syphilis where it assumed a milder form, and remained unilateral. Verhaege remarks that it is impossible to conclude, from the examination of interstitial keratitis, whether it is due to acquired or hereditary syphilis. Trousseau states that acquired keratitis is nearly always unilateral, less liable to relapse, of a milder type and shorter duration, and more amenable to treatment. It would appear difficult to exclude the existence of late hereditary syphilis in such cases, and for all practical purposes interstitial keratitis may be regarded as one of the chief signs of hereditary syphilis.

Treatment.—The general treatment is that for syphilis in general. Terrien recommends mercurial injections of biniodide or gray oil. Fournier advises mixed treatment with mercury and iodide. The *local treatment* consists in the instillations of sulphate of atropin (4 grains to the ounce) several times daily to cause dilation of the pupil and prevent the formation of adhesions of the iris to the lens (posterior synechia). During the period of resolution calomel or yellow oxide of mercury ointment (10 per cent.) are useful.

Keratomalacia.—This is a rare condition, consisting in fatty degeneration of the cornea, causing dulness of the surface. The infiltration may destroy the cornea in a few hours by a process analogous to that seen in neuro-paralytic keratitis. This condition is due to deficient nutrition of the cornea, and may be caused by other affections than hereditary syphilis, but the latter is the principal factor. The prognosis is grave, and in the most favourable cases permanent opacities are left.

Choroido-retinitis.—In late hereditary syphilis, according to Fournier, choroido-retinitis may occur which is identical with that met with in the acquired disease.

Ophthalmoplegia Externa.—Paralysis of the muscles of the eye is rare in hereditary syphilis, but a progressive form

of ophthalmoplegia externa may occur, gradually affecting all the muscles of the eye and the levator palpebræ. The ciliary muscle and the sphincter of the iris are nearly always unaffected. The paralysis is usually bilateral, and appears to be of nuclear origin.

The Ear.

Syphilitic lesions of the throat may cause symptomatic deafness by extension to the Eustachian tubes, and suppurative otitis media may also occur in infants with hereditary syphilis. But the true syphilitic deafness is a peculiar affection of the internal ear, causing total deafness.

Syphilitic Deafness.—This is described by Fournier as 'a deafness which establishes itself without the accompaniments of ordinary otitis, and without lesions capable of explaining it; which occurs suddenly with extraordinary rapidity; which attains considerable intensity in a short time; and which usually persists, permanently rebellious to all treatment.'

A child or adolescent begins to hear badly with one ear, and literally from day to day hears less and less, till in a few weeks he hears nothing at all with this ear. After an interval the other ear is affected in the same way, and the patient becomes stone deaf. There is no fever, pain, or local symptom, and no premonitory symptom of any kind. Nothing objective is found on examination of the ear.

The relation of this form of deafness to syphilis was established by Hutchinson. It is most common in hereditary syphilis at the same period at which keratitis usually occurs, but it may also occur in the acquired disease, and has been observed in tabes. The affection is usually bilateral, sometimes simultaneous, but occasionally with an interval of several years. It is often associated with subjective noises in the ear, such as hissing and buzzing, and with vertigo.

The pathology of this affection is not determined. Hutchinson regarded it as a neuritis of the terminations of the auditory nerve in the labyrinth, but Fournier thinks it more likely to be a lesion of the nerve centres, possibly of the floor of the fourth ventricle at the point of origin of the auditory nerves.

In a case which died of intercurrent disease, Moos has found some cell infiltration in the cellular tissue between the bone and the membranous wall of the vestibule, being most marked in the organ of Corti. The auditory nerve was normal. This points to a lesion of the labyrinth, but a single post-mortem is not sufficient to decide the question.

The affection is usually rebellious to treatment, but Fournier has recorded a case which was much improved by calomel injections, combined with the internal administration of iodides. Hutchinson also reports a case which was cured under specific treatment.

Deaf-mutism.—Some time ago Dalby stated that 'after scarlatina, hereditary syphilis is the most common cause of deaf-mutism.' Fournier also drew attention to this fact. This condition may be congenital, or may occur later after the child has learnt to talk. In the latter case the child speaks less and less because it cannot hear, owing to syphilitic deafness; it forgets words it formerly learnt, and finally does not speak at all. The child becomes dumb because it is prematurely deaf. According to Edmond Fournier, deaf-mutism sometimes alternates with other dystrophies of heredo-syphilis in the same family. Observations, however, on deaf-mutes are deficient, owing to the fact that they drift into asylums where syphilis is not studied.

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CHAPTER XX

SYPHILIS OF THE THIRD GENERATION

ALTHOUGH Van Helmont in the sixteenth, and Raulin and Sanchez in the seventeenth century, believed that syphilis might be transmitted through several generations, it is not till quite recently that the transmission of syphilis to the third generation has become an established fact.

Jonathan Hutchinson (who now disbelieves in transmission to the third generation) in 1865 reported two cases of heredo-syphilitic children issued from undoubtedly heredo-syphilitic mothers; but as the father's condition does not appear to have been fully investigated, the cases were not complete. About the same time Boeck of Christiania published a case which appears to be conclusive, and since then numerous cases have been reported, many of which fulfil all the conditions required. In 1900 the subject of transmission to the third generation formed the subject of a special discussion at the Medical Congress at Paris, at which considerable evidence was brought forward by Barthélemy, Tarnowsky, Jullien, Finger, and others. More recently this subject has been thoroughly investigated by Edmond Fournier and Tarnowsky and R. W. Taylor, of New York, has added further evidence.

In dealing with this question there are two conditions to be considered—(1) the transmission of the dystrophic effects of syphilis to the third generation; (2) the transmission of active syphilis, giving rise to virulent lesions. All competent authorities are agreed on the first question, but opinions differ as to the second. Tarnowsky holds that virulent syphilis is only transmitted to the third generation when there is reinfection of the heredo-syphilitic genitor with acquired syphilis. To this he gives the name of *binary syphilis*.

The recent inoculation experiments of Neisser and the researches on the *Spirochæta pallida* tend to show that, from the pathological point of view, transmission of active syphilis to the third generation is quite possible.

1. Neisser has shown that the organs of heredo-syphilitic subjects, including the *ovary*, give positive results when inoculated in monkeys.

2. Neisser has also obtained positive results from inoculation of monkeys with gummata in the tenth and seventeenth years of syphilis.

3. Levaditi has shown that the *Spirochæta pallida* is present in the organs of heredo-syphilitic infants, and in cases of late heredo-syphilis.

4. Schaudinn found the spirochæte present in a gumma of ten years' date.

All these facts show that the ovaries of a heredo-syphilitic infant may be infected with the spirochæte, and that this organism is capable of virulent action for a sufficient time to account for transmission to the third generation.

In order to prove transmission to the third generation the following conditions must be fulfilled:

1. The presence of acquired syphilis in one of the grandparents (first generation).

2. The presence of undoubted heredo-syphilis in one of the parents (second generation).

3. The presence of heredo-syphilis in the child (third generation).

4. The absence of acquired syphilis in either parent.

5. The absence of reinfection of the heredo-syphilitic mother with acquired syphilis (*vide* p. 46).

6. The absence of the intervention of another syphilitic genitor.

7. The absence of acquired syphilis in the child.

The most difficult of these conditions to fulfil is to exclude the intervening genitor; for the child of a heredo-syphilitic mother may be infected by paternal transmission, and thus form an example of ordinary heredo-syphilis of the second generation, and not one of transmission to the third generation through the mother. In other words, even if acquired syphilis

has been excluded in the supposed father of the child, the latter may be the syphilitic offspring of another man, so that the chain of transmission is interrupted and the value of the evidence destroyed.

Edmond Fournier has collected 116 cases from various sources and submitted them to a critical inquiry. He regards fifty-nine of these cases as fulfilling all the conditions mentioned above, and true examples of transmission from grandparents to grandchildren. In the other cases there was no mention of acquired syphilis in the grandparents, so that the evidence was less complete. In two cases the conditions were fulfilled by the establishment of acquired syphilis in the grandparents and hereditary syphilis in the parents and children; but the chain of evidence was complicated by the addition of another factor—viz., contamination of the mother with acquired syphilis. In these cases it was impossible to tell if this occurred before or after the birth of the child in question.

The results of the pregnancies in the 116 cases of transmission to the third generation are instructive, and show the following figures:

Out of 367 pregnancies there were 118 abortions, 59 early deaths, and 192 survivors—a mortality of 48 per cent. Of the 192 survivors, only 31 appeared to be free from all trace of hereditary syphilis.

The remaining 161 all showed various stigmata of heredosyphilis, *and* 28 *had active lesions*. The signs most frequently observed are given in the following table:

Infantilism (senile aspect, retarded speech, walking, and dentition)	45 cases
Lesions of the skeleton (rickets, exostosis, reduced height)	43 ,,
Ophthalmic stigmata	42 ,,
Lesions of the nervous system (meningitis, convulsions, arrest of intellect)	39 ,,
Dental stigmata (erosions and dystrophies)	36 ,,
Malformation of cranium	36 ,,
Ear symptoms (otitis and deafness)	13 ,,
Coryza	10 ,,
Microcephalus	5 ,,
Headache	5 ,,

The ocular stigmata were the same as those which occur in ordinary heredo-syphilis (second generation), and included rudimentary stigmata of the fundus, keratitis, irido-choroiditis, and choroido-retinitis.

Among the affections of the nervous systsm, meningitis and convulsions occurred most frequently, and after these, various neuropathic and psychic disorders.

The dental stigmata included all those met with in the second generation, and Hutchinson's teeth were observed in eight cases.

Other stigmata, which were met with occasionally, included scoliosis, arthropathies, spina bifida, congenital dislocation of the hip, talipes, genu valgum, pseudo-Pott's disease, asymmetry of the body, giantism and dwarfism, pelvic deformity, strabismus, myopia, astigmatism, glaucoma, coloboma iridis, idiocy, incontinence of urine, Little's disease, Friedreich's disease, hemiplegia, vertigo, hysteria, epilepsy, dementia, microcephalus, hydrocephalus, deformed ears, deaf-mutism, cardiac malformations, congenital amputations, ichthyosis, hypospadias, atrophy of the testicle, etc.

Fournier does not affirm that these stigmata are special to hereditary syphilis, and does not deny that they might be due to other infections; 'but observation appears to show that these stigmata have been noted in hereditary syphilis of the second generation (syphilis of the third generation) so frequently that they may be regarded as an expression of ancestral syphilis.'

Examples of Transmission of Virulent Hereditary Syphilis.—Edmond Fournier brings forward the following case in support of the transmission of active syphilis to the third generation. This case concerned a young man of twenty-two who had an extensive tuberculo-ulcerative syphilide of the thigh, which had been present since the age of five years; besides this he had multiple stigmata of heredo-syphilis, including both dental and ophthalmic stigmata, ichthyosis, etc.

The father of this patient also exhibited signs of heredo-syphilis, including the remains of old keratitis, dental erosions, ophthalmic stigmata, ichthyosis, an exostosis on the clavicle,

puny stature, etc. The paternal grandmother (first generation), after having had two healthy children, suckled a strange infant, which died 'with large suppurating sores on the body.' Soon after this a sore developed on her breast, followed by sores on the body. Her own child also developed similar sores, and died in a few weeks. She suffered afterwards from severe headaches, and eventually died of hemiplegia. Two years after this infection the child was born described above as the father of the original case. Fournier concludes that the grandmother contracted syphilis by suckling a syphilitic infant; that acquired syphilis was absent in the father and son; that there was no reinfection of the second generation; that the case fulfils all the conditions required, and shows the transmission of both the dystrophic and *virulent* effects of heredo-syphilis to the third generation.

E. Fournier also quotes the following cases, which appear to show transmission of virulent heredo-syphilis:

Case of Spillman and Etienne.—The grandfather was syphilitic; the father had heredo-syphilis; he was free from acquired syphilis, and married a healthy woman. This marriage resulted in 15 pregnances, which ended in 5 abortions, 2 early deaths, and 8 survivors. Of these, 1 appeared healthy, 6 had stigmata of heredo-syphilis, and 1 had, besides these, cicatrices of the buttocks, buccal ulcerations, and a perforation of the soft palate.

Lemonnier's Case.—Grandfather syphilitic; father heredo-syphilitic, and married to a healthy woman. From this marriage there were two children. One of these, a man of twenty-seven, had slight stigmata of the paternal heredity; never had acquired syphilis, but had a gumma of the nose and syphilitic testicles. The second child, aged twenty-four years, showed no hereditary stigmata, and had never contracted syphilis, but had ulcerating gummata on the legs.

Pospelow's Case.—Grandfather syphilitic; father heredo-syphilitic, and married to a healthy woman. Ten children, of which eight survived. One of these was puny and had Hutchinson's teeth; also a perforation of the nasal septum and ulceration of the palate.

Chirivino's Case.—Both paternal and maternal grandmothers had acquired syphilis. The father and mother were both heredo-syphilitic and free from acquired syphilis. One child, puny and hydrocephalic, had also a palmar and plantar syphilide.

E. Fournier has collected nineteen cases of the same kind, in which he believes that all the conditions required to prove transmission of syphilis to the third generation were fulfilled. The virulent manifestations observed in these cases included papular syphilides in six cases; ulcerated gummata of the nose, legs, and breast in six cases; palmar and plantar syphilides in four cases; syphilitic sarcoceles in four cases; ulcerative syphilides and mucous syphilides in one or two cases.

Boeck's Case. — The grandmother (first generation) was treated for secondary syphilis in 1854; the mother (second generation) in 1860 for hereditary syphilis at the age of two months; the child (third generation) in 1889, when five months old, for typical hereditary syphilis, with coryza, plantar and palmar syphilides, etc. The mother at this time showed scars about the mouth and Hutchinson's teeth, but had no sign of acquired syphilis. The father was examined, but showed no signs of syphilis. The child in question was the second, the first being healthy. Also there was another healthy child begotten by another father a year before marriage. The objection which might be raised in this case is, of course, the possibility of paternal heredity, and of the first child after wedlock being procreated by the same father as that of the child born before marriage. In other words, the syphilitic child might have been procreated by the father by paternal heredity, while the first two children were the offspring of another man. However, according to Professor Fournier, cases occasionally occur where healthy children precede syphilitic ones.

R. W. Taylor's Cases.

'*Case* 1.—The grandmother was a perfectly healthy woman, and was married in 1869 to a man whose history I never could obtain, but who acknowledged that he had chronic rheumatism, and that he had taken

potassium iodide for years. In later years he suffered from cardiac disease, and died of nephritis. Several months after marriage the wife became syphilitic, and presented severe, varied, and extensive secondary symptoms, which were quickly followed by gummatous tumours and abscess of the arms and legs. She also suffered from perforation of the hard palate. She was a woman in whom the infection seemed to run riot, and was most careless and indifferent in following treatment. After severe ordeals she, in later years, lost all evidences of syphilis and became hearty and strong.

'In 1871 this woman, who is the first genitor, in the second year of her active syphilis became pregnant, and in 1872 had a girl baby. For a time she took antisyphilitic treatment, but not in an active and persistent way.

'The baby was not markedly thin or anæmic, though it had typical snuffles, roseola, mucous patches of the mouth and genitals, and typical syphilitic pemphigus of the palms and soles. She had a relapse within a year of generalized papular syphilides. Under treatment administered in a haphazard manner this baby became seemingly healthy, presented no visible lesions or sequelæ, and at her fifth year it was noted that she seemed healthy, had gradually gained in weight, and seemed well nourished. This child had no further treatment whatever, and her mother looked upon her as thoroughly cured. (The mother had two other children, a boy and a girl, who never gave any evidence of specific taint.)

'The woman's daughter grew up to be a large, big-boned, strapping girl, who was married to a perfectly healthy man (well known to me) in 1888. She has never been infected with acquired syphilis.

'In two years she had a baby girl at term, the victim of syphilis in the third generation, which was thin, weakly, and atrophic, and was only raised with great difficulty, and suffered from gastro-intestinal disorders, mild broncho-pneumonia, and marasmus. Under careful hygiene, change of air, and proper medication this child became much improved. In 1896, however, I found her with Hutchinson's teeth, double mild keratitis, and deafness in one ear. In the following five years she had swellings of the sternum, clavicles, both radii, and ulna and tibiæ. In 1902 she began to develop subcutaneous nodules on the arms and thighs, and later on on the legs. These lesions increased in size, became adherent to the skin, ulcerated, and presented a typical picture of late gummata, such as we see in acquired syphilis. When examined recently the child, being twelve years old, was very small for its age, not very acute in intellect, atrophic, and in general puny and unwholesome. She needs the greatest care, and constantly suffers from gastric and intestinal disorders, and is very prone to catch cold.'

This case may be summed up as follows:

'1. Grandmother infected with syphilis in 1869; had secondary and tertiary lesions of much severity. She was careless of treatment. She was the first genitor.

'2. In 1872 this woman gave birth to a girl baby which presented classical hereditary syphilitic symptoms. After many vicissitudes this child (the second genitor) grew up seemingly healthy and strong, and never having been infected with acquired syphilis, she in two years gave birth to a baby daughter.

'3. In 1890 this second genitor gave birth to a miserable weakling girl, atrophic, marasmic, with very little strength and vitality, who at birth gave no distinct evidence of hereditary syphilis (third generation), but who in five years developed true dystrophic symptoms: Hutchinson's teeth, keratitis, ear troubles, and osseous swellings, and later on unmistakable evidence of a virulent form of late syphilitic infection (third) in characteristic gummatous tumours and ulcers.

'This third syphilitic by inheritance is now growing up a victim of infantilism and general atrophy.

'It will thus be seen that all the pathological links necessary to undoubtedly prove a case of syphilis lasting to the third generation are furnished by the recital of this lugubrious history involving three females.'

'*Case* 2.—A syphilitic man, aged twenty-four, who had been infected two years previously, and who was indifferent in following treatment, married a healthy young woman in 1868. Within two years this woman became syphilitic and pregnant. She and her husband were neglectful in the matter of treatment, and in 1870 she gave birth to a syphilitic male child with all the classical symptoms of inherited infection. The child was tolerably well treated for a time, but when four years old he was brought to me again with Hutchinson's teeth, opacity of the cornea, stunted nose, and marked cicatricial fissures at the angles of the mouth. In the course of time he became reasonably strong and healthy. His intellect was remarkably keen, and he developed into an alert lad, very proficient in business. His mother realized at last the necessity of treatment for herself and the boy, and the latter was treated on and off for six or seven years. This lad grew to manhood, and was not infected with acquired syphilis at any time. I am certain of this point, since I knew the whole family so well. The mother had three children subsequently, none of whom presented any blemish. She had no miscarriages.

'When the young man was twenty-five years old, in 1894, he married a perfectly healthy girl, aged eighteen, who never presented any evidence of syphilis at any time. The young man (the second genitor) remained healthy, bright, and strong.

'Three years after their marriage (1897) the wife gave birth to a rather thin, unwholesome-looking girl, who presented no syphilitic lesions whatever. This girl grew up weak and ailing, suffered much from bronchitis, and in summer from diarrhœa. She remained rather thin and much undersized, but intelligent and vivacious. Her teeth were not typical of inherited infection, but they were irregular and stunted. When five years

old arthritis of the knees, one elbow, and the sterno-clavicular articulation caused the patient much suffering. Later on there was periostitis of both tibiæ and one radius, which was also very painful. By my direction mercurial ointment was rubbed over the affected surfaces, and potassium iodide was given in liberal doses. The first effect of this treatment was magical, and with every recrudescence, of which there were several, it was repeated. The result was that in about five years this girl seemed to take on new life. She grew in stature, in flesh, and in general well-being, and to-day is well nourished, lively, and buoyant, and bids fair to be a comely, healthy girl. She was evidently the victim of syphilitic heredity.

'The contrast between the condition of the father in early years and that of his daughter was very striking. The one was an hereditary syphilitic, the other was the victim of syphilitic heredity.'

Summary:

'1. A healthy woman, married to a man, syphilitic two years, contracted syphilis two years later coincidently with the development of pregnancy.

'2. She gave birth to a male child who soon after birth was characteristically heredo-syphilitic, and later developed typical undoubted evidences of inherited taint, which showed themselves for several years. He never was infected with acquired syphilis. He married a healthy girl.

'3. Three years after the marriage of this second genitor the wife gave birth to a thin, weakly girl, who presented the appearances of infantilism. At four years many dystrophic symptoms of the bones and joints developed and were promptly cured by antisyphilitic treatment. This case, therefore, was a clearly-marked illustration of the development of syphilis in three generations. In the first, active syphilis; in the second, virulent hereditary syphilis; and in the third a dyscrasic condition attended with well-marked dystrophic changes.'

Tarnowsky has made comprehensive study of syphilitic heredity, based on prolonged observations during many years; his chief conclusions are as follows:

'1. Syphilitic heredity manifests itself in three ways: by manifestations peculiar to hereditary syphilis, by dystrophic influence, and by an acquired immunity.'

'2. It is in the second generation of the syphilitic family that the hereditary influence of acquired syphilis declares itself with the greatest intensity, in causing a considerable number of abortions, still-births, infants who succumb after a few months of existence, and infants afflicted with signs of hereditary syphilis or different dystrophies.'

'3. Immunity of the second generation (Profeta's law) is generally only temporary.'

'4. The influence of syphilitic heredity diminishes sensibly in the third generation. This attenuation shows itself in the diminished number of abortions, still-births, and infants who die early; by the absence of phenomena in the third generation; and by the considerable diminution in the number of dystrophies, as well as their qualitative attenuation.'

'5. Acquired syphilis of the first generation is not transmitted to the third in the form of the recognised phenomena of hereditary syphilis. Syphilitic heredity, descending from the second to the third generation, manifests itself exclusively by a dystrophic influence.' (In other words, Tarnowsky does not support the transmission of virulent syphilis to the third generation.)

'6. Transmission from the grandparents to the grandchildren by skipping a generation when the second generation have escaped syphilis has not been proved, and it is doubtful if it occurs.' This view is also held by Alfred Fournier.

'7. The dystrophic influence of acquired syphilis is not in proportion to the severity of the lesions; but the dystrophic influence of the second generation corresponds generally with the degree of the degeneration in the genitors.'

'8. When the second generation is not affected with the symptoms or dystrophies of hereditary syphilis it generally produces a healthy progeny.'

'9. Dystrophies of the second generation are not transmitted in the same form to the third generation.'

'10. Lesions of hereditary syphilis in the third generation (virulent lesions of Fournier) occur when there is new syphilitic infection of the second generation' (to this Tarnowsky gives the name *binary syphilis*). 'This may also occur when a representative of the second generation marries a subject with acquired syphilis.'

'11. Binary syphilis exerts on the third generation a much more fatal influence than syphilis of the first on the second generation. There are a greater number of abortions, still-births, and early deaths, and the proportion of hereditary

syphilitic phenomena and dystrophies is increased. Binary syphilis is one of the principal causes of the rapid degeneration of the population of country districts.'

'12. The supposed progressive attenuation of syphilis in proportion to the syphilization of the population is not supported by fact.'

'13. The evil hereditary influence of acquired syphilis of the first generation manifests itself with the greatest intensity in the second generation, diminishes considerably in the third, and becomes absent in the fourth generation. Syphilis has an incomparably more fatal influence on the species and on society than on the individual.'

R. W. Taylor states that 'death without apparent cause is peculiar to the syphilitic children of the third generation. Abortions and miscarriages are rarer in the third generation, and do not constitute a pathognomonic sign as in hereditary syphilis of the previous generation. As a rule, syphilitic infants of the third generation in the first six months of life do not present any characteristic anomaly, and they may appear healthy for several years (two to five), and then without appreciable cause they become thin, and their intellectual and physical condition is more or less stunted. Intercurrent affections very often mask the syphilis and tend to a fatal termination.'

Conclusion.—Such is the evidence up to the present time concerning the transmission of syphilis to the third generation. Human beings cannot be kept under constant observation while breeding, like animals, and therefore absolute elimination of all the possible flaws in the evidence is impossible. Also it is the good fortune of few of us to be able to follow up many cases for three generations. There appears, however, to be sufficient evidence to justify the following conclusions:

1. That the degenerative or dystrophic effects of syphilis are frequently transmitted to the third generation, and possibly further, only to die out with eventual sterility.

2. That, although difficult to prove, the transmission of virulent hereditary syphilis to the next generation is possible,

and depends chiefly on the two factors of *time and treatment*. We know that the signs of late hereditary syphilis may be delayed till the procreative age; hence a heredo-syphilitic genitor in a virulent state might transmit the disease in a virulent form to the offspring. The reason why such cases are not more common lies in the fact that comparatively few subjects marry while suffering from hereditary syphilis in an active state. At the time of marriage the disease is usually attenuated by time, and also by treatment, if this has been properly administered.

3. That reinfection of a heredo-syphilitic genitor increases the virulence of the disease and its fatal effects on the offspring (binary syphilis of Tarnowsky).

4. That the two chief obstacles to actual proof of transmission to the third generation are the possible reinfection of the second generation, and the possible intervention of another syphilitic genitor. The intervening genitor is always a stumbling-block in the elucidation of the problems of heredity; for, although a child is obviously the offspring of its mother, paternal parentage is seldom capable of scientific proof.

5. That the hereditary transmission of syphilis is one of the chief factors in physical, mental, and moral degeneration.

When we consider that syphilis has the greatest tendency of all diseases to hereditary transmission; that this transmission may reach the third generation; that the disease is frequently unrecognised, wilfully concealed, or wrongly diagnosed; that in a certain percentage of cases syphilitic infection is contracted accidentally (syphilis insontium); and that the majority of cases are insufficiently treated, it is difficult to conceive that many families in 'civilized countries' can altogether escape some trace of the syphilitic taint.

The reason why cases of transmission to the third generation are not more frequently recorded is that the class of medical men who have most opportunities for observing such cases—the family practitioners—are not as a rule syphilologists.

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CHAPTER XXI

GONORRHŒA

Gonorrhœa is an infectious disease caused by a pathogenic microbe—the *gonococcus*. It usually affects the mucous membrane of the genito-urinary organs — the urethra and its annexes in the male, and in the female the vagina, cervix uteri, and urethra. The specific inflammation may extend from the urethra to the prostate, testicles, vesiculæ, and bladder in the male, and in the female to the uterus, Fallopian tubes, ovaries, and peritoneum. The disease is at first a local one, but often becomes generalized by dissemination of the gonococci or their toxins throughout the system.

Gonorrhœa is usually, but by no means always, of venereal origin, and infection may be conveyed in some cases by means of contaminated linen, towels, instruments, etc. Gonorrhœa occurring in pregnant women is the cause of purulent ophthalmia in the newborn infant (ophthalmia neonatorum), and sometimes causes purulent rhinitis.

Gonorrhœa is thus not confined exclusively to the genito-urinary organs, and, besides the eye, the specific inflammation may affect the rectum, the nose, and the mouth, giving rise to gonorrhœal rectitis, rhinitis, and stomatitis.

Gonorrhœa was formerly confounded with syphilis (*vide* Chapter I.), but was separated as an entity by Ricord. He, however, denied the virulent nature of gonorrhœa, and regarded it as a simple catarrh produced by various irritations, such as menstrual discharge, lochia, leucorrhœa, irritating injections, strong drinks, sexual excess, etc.

In 1879 Neisser discovered the gonococcus in urethral and conjunctival gonorrhœa. This result was confirmed by Bokai

and Finkelstein, who also cultivated the microbe and reproduced acute urethritis by inoculation of cultures. Zweifel, Bumm, and Welander soon afterwards demonstrated that the lochial discharge of women was incapable of causing conjunctivitis in newborn infants unless it contained gonococci. De Christmas isolated a *gonotoxin* which caused gonorrhœal urethritis when injected into the urethra.

The Gonococcus.—This micro-organism is a diplococcus, which appears bean or kidney shaped under high magnification. Each pair is enclosed in a capsule. The gonococcus is easily stained by methylene blue and other aniline dyes, and is decolorized by Gram's method. A characteristic feature is the *intracellular* position of the cocci inside the pus cells. The cocci are also seen outside the pus cells, especially in the later stages.

CULTIVATION.—The gonococcus will not grow on ordinary media, such as agar, gelatin, peptone, or bouillon, but can be cultivated on serum mixed with twice its volume of agar, or on blood-agar. The temperature must not be above 38° C., as the gonococci are injured or destroyed at a temperature of 39° to 40° C. On the other hand, the temperature must not be below 36° C., as the agar is then coagulated. Neisser uses a mixture of 1 part ascitic fluid and 2 parts agar, with 1 per cent. peptone.

Bumm found that the transference of a twentieth culture of the gonococcus, when inoculated on the healthy urethral mucous membrane, caused acute urethritis, the pus of which contained gonococci. Inoculation in animals, on the other hand, has so far been negative.

The gonococcus develops on all kinds of epithelium of mucous membranes. It penetrates the cells and intercellular spaces, especially of cylindrical epithelium, causes desquamation of the epithelial cells, and attraction of leucocytes, into which it penetrates and multiplies. It causes suppuration in the epithelial layers, and also in the subepithelial connective tissue. It penetrates the lacunæ and glans of the urethra, in which it may remain for a long time latent (*latent gonorrhœa*), but liable to recrudescence, causing reinfection of the urethra.

PLATE IV.

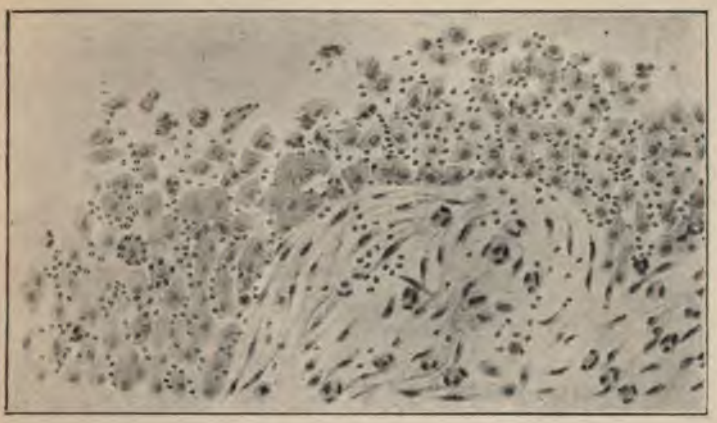
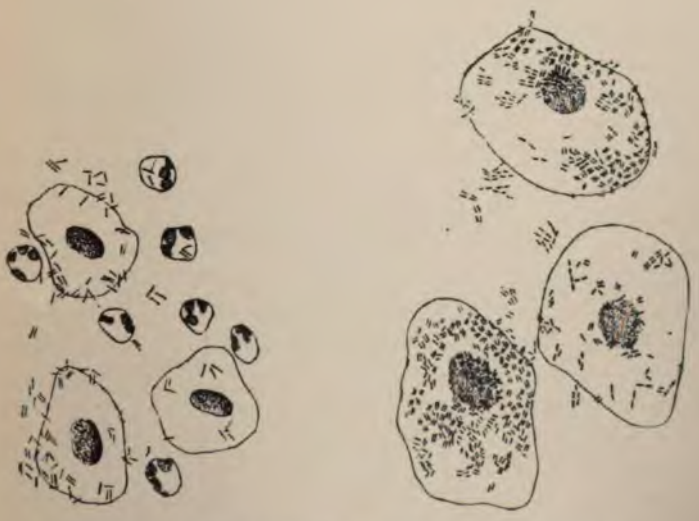


FIG. 1.—SECTION OF URETHRA, SHOWING INVASION OF EPITHELIUM AND SUBEPITHELIAL TISSUE BY THE GONOCOCCI.



FIGS. 2 AND 3.—PSEUDO-GONOCOCCI. (AFTER FINGER.)

In the vaginal mucous membrane of adult women the gonococcus does not develop with such vigour as in the male urethra, but multiplies chiefly in the cervix uteri, Bartholin's glands, and the urethra. In young girls and infants, however, the vaginal mucous membrane is more delicate, and is more severely attacked by the gonococcus.

The gonococcus has been found in all the primary gonorrhœal inflammations of the genito-urinary organs, conjunctiva, rectum, nose, and mouth; and in general gonorrhœal infection in the lymphatic glands, joints, endocardium, synovial sheaths, pleura, and peritoneum, and in the blood during life.

The gonococcus may retain its vitality for many years. It may be present in comparatively insignificant discharges, and may be absent in severe complications. According to Neisser, most cases of acute gonorrhœa are contracted from chronic cases.

Gonococci which have lain dormant in the male urethra may become active when transplanted to a virgin vagina, and may reinfect the male urethra from which they originated. In this way a man may be reinfected with his own gonococci by rejuvenating them on a virgin vagina. A husband who has considered himself cured of his old gonorrhœa before marriage may thus blame his wife for his misfortunes, whereas he has reinfected himself and probably infected her. It is obvious that such a state of affairs may lead to a multiplicity of matrimonial, social, and legal complications.

Extragenital Gonorrhœa.

Gonorrhœal Ophthalmia.—Gonorrhœal pus when inoculated on the conjunctiva gives rise to a severe form of acute purulent ophthalmia. Infants are often affected during birth from gonorrhœal affection of the mother, and this *ophthalmia neonatorum* is responsible for many cases of total blindness. Morrow states that from 20 to 30 per cent. of total blindness in the United States is due to ophthalmia neonatorum. It has been shown that the lochial discharge in women is incapable of causing ophthalmia in newborn infants unless it contains gonococci.

Symptoms.—The eyelids become red, swollen, and œdematous, and cannot be opened; there is much swelling of the palpebral and ocular conjunctiva (chemosis), and pain is usually severe. This condition is soon followed by abundant purulent discharge and infiltration of the ocular conjunctiva. In severe cases ulceration and sloughing of the cornea, iritis, and panophthalmitis occur; but mild cases sometimes occur in which the symptoms are difficult to distinguish from simple catarrhal conjunctivitis. Diagnosis can, however, be usually decided by the presence of the gonococcus in the discharge.

Inoculation of the conjunctiva may take place through the medium of the fingers or towels, etc., contaminated with gonorrhœal discharges.

Treatment.—The sound eye (if only one eye is affected) must be protected from infection from the diseased eye. This may be done by means of a Buller's shield, which consists of a watch-glass enclosed between two pieces of adhesive plaster, with a hole cut in the centre. This is fixed along the nose, forehead, and cheek, leaving a space for ventilation at the outer side. This apparatus enables the patient to see, and allows the surgeon to examine the eye without disturbing the dressings on the other eye.

The affected eye should be irrigated every hour with a solution of 1 in 5,000 *perchloride of mercury*. If the lids are too stiff to be separated by retractors, the outer canthus must be divided with scissors as far as the outer angle of the orbit. This relieves tension and pressure on the globe, diminishes pain, and enables the surgeon to separate the lids and irrigate the palpebral sac. Iced-water dressings should be applied during the intervals of irrigation. When suppuration has set in, the conjunctiva is treated with a 2 per cent. solution of *nitrate of silver*, applied daily with a small brush after irrigation and drying. The nitrate of silver solution is allowed to remain for about a minute, and is then washed off with perchloride solution. Atropin drops should also be applied ($\frac{1}{2}$ per cent.) to keep the pupil dilated, and also to relieve pain.

When there are *corneal ulcers* which do not quickly yield to the above treatment, they should be touched with the galvano-

cautery, applied at a dull red heat. This should be applied to the whole floor of the ulcer and the healthy edges around it. If the ulcer is deep, the instrument may perforate the cornea. If hypopyon already exists, this causes no harm, but otherwise it is better to leave Descemet's membrane intact, and prevent protrusion of the iris.

Ophthalmia neonatorum usually occurs on the third day after birth, but cases of *ante-partum ophthalmia* have been recorded, generally in cases of protracted labour in which the membranes were ruptured some time before birth. The symptoms are the same as in gonorrhœal ophthalmia occurring later in life, but are as a rule less acute. Both eyes are usually affected, and the treatment is the same as that described above, but in severe cases the nitrate of silver should be applied twice daily.

Prophylactic treatment of ophthalmia neonatorum consists in disinfecting the mother's vagina with 1 in 1,000 perchloride of mercury during parturition, carefully washing the infant's eyes, and instilling a drop of 2 per cent. nitrate of silver into each eye. This method, known as *Credé's method*, is adopted as a routine procedure at some lying-in hospitals; at others the eyes are irrigated with a 1 in 5,000 solution of perchloride of mercury immediately after birth. This prophylactic treatment has diminished the frequency of ophthalmia neonatorum, and if it was more universally adopted there would be less candidates for the blind asylums.

Gonorrhœal ophthalmia may give rise to general gonococcal infection, just the same as gonorrhœa of the genito-urinary organs. In twenty-three cases of gonorrhœal arthritis in infants reported by Clement Lucas no less than eighteen originated from ophthalmia neonatorum.

Gonorrhœal Rhinitis.—This may also be contracted by the infant during birth, in the same way as ophthalmia, from gonorrhœa of the mother. Treatment consists in irrigation of the nostrils with permanganate of potassium.

Gonorrhœal Stomatitis.—This has been reported as occurring after *coitus ab ore*, and has also been found in newborn children. The lesions consisted in gingivitis and erosions

of the tongue and palate, in which gonococci were found. Kimball has reported cases of general gonorrhœal infection which apparently originated in the mouth.

Gonorrhœal Rectitis.—Anorectal gonorrhœa is not uncommon as the result of sodomy, but it may also be caused by contaminated instruments, such as enema syringes, etc. The symptoms consist in pain on defæcation, with tenesmus; redness, erosions, and even ulceration of the mucous membrane; purulent discharge, and sometimes vegetations. Rectal gonorrhœa may be complicated by abscesses, fistula, and phlebitis. Chronic rectitis may lead to fibrous thickening and stricture of the rectum. Anorectal gonorrhœa may be complicated by gonorrhœal rheumatism. Treatment consists in irrigations with permanganate (1 in 4,000) or perchloride of mercury (1 in 1,000), iodoform suppositories and ointment.

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CHAPTER XXII

GONORRHŒA IN THE MALE

Acute Urethritis.

ACUTE GONORRHŒAL URETHRITIS, or 'clap,' is due to the introduction into the urethra of matter containing the gonococcus. This has been proved by experimental inoculation from cultures of the gonococcus, and distinguishes gonorrhœal from other forms of urethritis.

The disease is usually contracted by sexual connection with a woman affected with gonorrhœa of the genital organs. In some cases infection may be due to contaminated towels and linen, or matter deposited on the seats of water-closets. The last method of contagion is often put forward by patients as an excuse to cover their lapse from the path of virtue, and is usually received with ridicule; nevertheless, contamination by public water-closets, although comparatively uncommon, does not belong to the realms of fable. In cases of sodomy gonorrhœal urethritis may be contracted from rectal gonorrhœa in the passive pederast.

Anatomy of Urethra.—The meatus is the narrowest part of the urethra; after this comes the dilatation of the fossa navicularis; then the penile urethra, which is of uniform calibre; then the bulb, which is the widest part; then the membranous urethra, which is narrower; lastly the prostatic urethra, which becomes narrow at the neck of the bladder. There are thus four constricted parts—the meatus, the end of the fossa navicularis, the membranous part, and the vesical orifice. The first two of these are the least dilatable.

The urethra is divided both anatomically and developmentally by the sphincter urethræ and membranous urethra

into two parts—an anterior and posterior. The posterior urethra is developed from the uro-genital sinus, the anterior from a grooved bud (the phallus) arising from the anterior wall of the cloaca. Owing to this division, secretions from the anterior part emerge by the meatus, while those from the posterior part regurgitate into the bladder. The sphincter also offers a certain amount of resistance to the passage of injections.

The mucous membrane contains numerous glands or follicles known as the glands of Littré, and cul-de-sacs or pockets known as the lacunæ of Morgagni. The latter are situated on the upper surface of the urethra, and the largest one, the lacuna magna, is situate near the fossa navicularis. The glands of Littré are small pin's-head glands which are not easily visible except when inflamed (Plate V.).

Pathology of Urethritis.—The meatus and fossa navicularis are lined by pavement epithelium, which resists the gonococci. The rest of the urethra is lined with cylindrical epithelium, through which the gonococci easily penetrate, and may reach the subepithelial tissue as early as the third day. The gonococcus causes separation and degeneration of the epithelial cells, and irritates the mucous membrane by its toxins. This leads to invasion of the mucous membrane by leucocytes (chemiotaxis) which phagocyte the gonococci and reach the surface as pus cells containing the cocci.

The damaged epithelium begins to regrow at the end of five or six weeks, but the cylindrical epithelium is never restored *ad integrum*. The cylindrical cells are transformed into flat, stratified, horny epithelium (keratinization), and the mucous membrane undergoes more or less sclerosis. Motz has shown that infiltration of the mucous membrane may persist for twenty or thirty years.

The *glands of Littré* may undergo one of three changes—(1) the same changes as the surface epithelium; (2) atrophy by periglandular infiltration; (3) cystic suppuration from plugging of the ducts.

In the *posterior urethra* the same epithelial changes occur; the ejaculatory ducts become constricted, causing pain on

ejaculation, and the rigidity of the ducts leads to escape of spermatozoa, which are often found in the secretion from chronic urethritis.

Urethritis is subdivided into *anterior urethritis* and *posterior urethritis*, according as the anterior or posterior urethra is affected. In acute gonorrhœa the process is at first usually confined to the anterior urethra, but seldom remains limited to it for long. Hence the distinction between anterior and posterior urethritis must not be pushed too far.

Balzer points out that the gonococcal invasion may extend to the posterior urethra with great rapidity, and that most cases of gonorrhœal urethritis affect the posterior urethra by the end of the third week, and sometimes in the second week. The inflammatory process is most marked in the fossa navicularis, the bulb, and the membranous urethra.

The bacteriological evolution of gonorrhœal urethritis may be divided into three stages—(1) a gonococcal stage which persists during the whole course of acute and part of chronic gonorrhœa; (2) a stage of secondary infection with other micro-organisms, towards the end of the acute period; (3) an amicrobial stage consisting of simple catarrh.

Symptomatology.—The incubation period of acute gonorrhœa, in a virgin case, averages two to five days, but may be as long as two or three weeks. The course of acute urethritis may be divided into three stages—a period of invasion, a stationary period, and a period of decline.

Period of Invasion.—In the first stage there is a slight mucoid discharge which glues together the lips of the meatus in the morning. This is accompanied by itching and smarting in the fossa navicularis. The meatus soon becomes red and swollen, and there is a variable amount of pain on micturition. This initial period lasts about a week. The urine contains pus cells with gonococci, and epithelial cells.

Stationary Period.—In the second stage there is profuse purulent discharge, especially at night, of a yellow or greenish-yellow colour, and sometimes blood-stained. The urine is turbid, and contains flakes of pus. Microscopical examination shows polynuclear leucocytes, eosinophiles,

neutrophiles, and lymphocytes; gonococci are found both free and in the leucocytes. Simple staining with methylene blue is sufficient to demonstrate the presence of gonococci in most cases, but in doubtful cases it may be necessary to decolorize with Gram's method.

Pain varies considerably in different patients; sometimes it is slight during the whole course of the disease, but more often there is a good deal of pain during micturition, and especially during erection at night.

If the anterior part of the urethra only is affected, when the patient urinates into two glasses, the first is turbid, while the second is clear. If the posterior urethra is affected—which is often the case towards the end of the second week and sometimes at the end of the first week—the urine in the second glass is also turbid. This proceeding is known as *Thompson's two-glass test.*

Posterior Urethritis.—According to Guiard and others, the posterior urethra is affected in 75 per cent. of cases of acute gonorrhœa. On examination of the urine by the two-glass test, the second glass contains mucus, filaments, and sometimes a little blood. This examination is best made with the morning urine, or, at any rate, after the patient has gone for several hours without making water.

Kromayer's test for posterior urethritis consists in injecting the anterior urethra with 4 or 5 c.c. of methylene blue (1 in 1,000), closing the canal for a few minutes, expressing the fluid, and then making the patient urinate. The filaments in the anterior urethra are stained blue; if white filaments are present, they come from the posterior urethra, and show the presence of posterior urethritis.

In some cases there is frequent desire to micturate, accompanied by urethral spasm and the passage of a few drops of blood at the end of micturition. In severe cases there may even be retention of urine. In cases of intense posterior urethritis the pain radiates to the perineum and rectum, and there may be pain on defæcation. When the inflammation extends to the corpus spongiosum, painful nocturnal erections occur, and the penis is curved with the concavity down-

wards. This condition is known as *chordee*, and is due to the unequal expansion of the corpus cavernosum and corpus spongiosum during erection, the latter being bound down by inflammatory exudation and acting as a tie-rod to the arc formed by the corpora cavernosa.

Complications.—In some cases of acute gonorrhœa the inflammation extends to the prostate, which may be tender and enlarged on rectal palpation. Other complications sometimes observed are œdema of the prepuce, dorsal phlebitis of the penis, lymphangitis, and occasionally suppurating inguinal bubo. These complications are rare, and are generally due to balanitis and secondary infections; but the gonococcus has been found in suppurating bubo.

In severe cases there are febrile symptoms, with rise of temperature and anæmia, etc. These symptoms are probably due to toxæmia, caused by the gonotoxin. In the blood during the acute period polynuclear leucocytosis and slight lymphocytosis have been observed.

When an acute fever, such as measles, pneumonia, etc., occurs during the course of acute gonorrhœa, the discharge ceases for a time, but usually recurs when the fever has abated. This is due to the fact, demonstrated by Finger, that the gonococcus loses its vitality at a temperature of 39° C., and is destroyed by a temperature over 40° C. An acute gonorrhœa might therefore be cured by an intercurrent attack of fever, provided the temperature rose sufficiently high to destroy the gonococci.

Period of Decline.—After the stationary period, which lasts about two or three weeks, comes the period of decline. The discharge diminishes in quantity, and becomes less purulent and more mucoid, but gonococci are still present in considerable numbers. The urine is less turbid, but contains opaque filaments formed of fibrin, leucocytes, and epithelial cells. These filaments are commonly known as 'clap-threads.' The painful symptoms and chordee subside with the diminution in the discharge, which is finally reduced to a mucoid discharge, gluing the lips of the meatus together in the morning (the 'morning drop' or *goutte militaire* of the French authors). The

period of decline lasts for two or three weeks on the average, but relapses sometimes occur, and some cases pass on to the condition of chronic urethritis.

Diagnosis.—Suppurative balano-posthitis may at first sight suggest gonorrhœa, but the pus does not emerge from the urethra and does not contain gonococci.

Secondary Infections. — Towards the end of an attack of gonorrhœal urethritis the gonococcus is often associated with secondary microbes. The normal urethra contains microbes which, although harmless in the normal state, may become noxious when the urethra has been damaged by the gonococcus. Among these micro-organisms are a bacillus resembling that of diphtheria, different forms of staphylococci, and the *Micrococcus candidans* (Pfeiffer).

The *Bacillus coli*, the streptococcus and the pneumococcus, and certain diplococci, may also give rise to urethritis which simulates gonorrhœa, and the diplococci are sometimes difficult to distinguish from gonococci. When the gonococcus is intracellular the diagnosis is easy; but when the cocci are few and extracellular, it may be necessary to resort to cultivations to confirm the diagnosis. Decolorization by Gram's method differentiates the gonococcus from most other urethral microbes, but Steinschneider and Galensky have described four species of diplococci occurring in the normal urethra, two of which are decolorized by Gram. However, decolorization by Gram's method is diagnostic of the gonococcus in about 95 per cent. of cases.

Non-microbial Urethritis. — Urethritis may be caused by the ingestion of certain medicaments, such as cantharides. Urethritis due to oxaluria, rheumatism, and gout has also been described, but must be received with a certain amount of scepticism. It is probable that most of these cases are explained by long-standing latent gonorrhœa. Masturbation has also been given as a cause of urethritis, but there is no apparent reason why this should give rise to urethritis any more than normal sexual connection.

Tuberculous Urethritis.—This is recognised by the presence of the tubercle bacillus in the discharge, and almost always

occurs in the posterior urethra. It is generally associated with tubercle of the prostate, vesiculæ, and testicles. Gonorrhœa may, however, occur in a patient suffering from genito-urinary tuberculosis.

Intra-urethral Chancre.—A discharge arising from an intra-urethral chancre may be mistaken for gonorrhœa, but the chancre can usually be felt somewhere near the meatus, and the discharge does not contain gonococci.

Prognosis.—The prognosis of acute gonorrhœal urethritis is favourable in the large majority of cases, but it should always be guarded, as general infection may occur in the early stages. When the inflammation extends to the posterior urethra, the danger is increased, and the patient is exposed to the dangers of prostatitis, epididymitis, gonorrhœal rheumatism, etc. A narrow meatus and hypospadias are unfavourable conditions for cure. Both the local and general infection are rendered more serious by the addition of secondary microbial infection.

As long as the filaments contain leucocytes and gonococci the case is not cured and the patient is still infectious. It is also possible that the patient may transmit infection after gonococci are absent from the filaments, and he should be regarded as possibly infectious as long as filaments are found in the urine. It must be remembered that, although a positive result of examination for gonococci confirms an infectious state, a negative examination does not exclude it. The gonococci may remain latent in the urethral follicles for very long periods, and may take on renewed activity at different times, according to the condition of health of the patient and his modes of life, etc. Therefore, as the presence of filaments in the urine is the only objective sign of the persistence of the gonorrhœal process, it is a good rule to consider a patient as possibly contagious as long as these are present.

In favourable cases acute gonorrhœa may end in thirty or thirty-five days, but in the majority of cases the affection lasts for six to eight weeks, and sometimes three months. The cases of so-called abortive cures of acute gonorrhœa which are reported from time to time must sometimes be looked upon as open to question.

Some patients never present the acute and painful stage of acute gonorrhœa, and the disease pursues a subacute course. In some cases there may even be gonococcal urethritis without purulent discharge, and the disease is thus only recognised by the presence of filaments in the urine, or by the development of some complication, such as epididymitis.

Chronic Urethritis.

Acute gonorrhœa, instead of undergoing resolution in six to eight weeks, may become chronic, constituting the condition known as *gleet*. In this condition there is a tendency to infiltration of the submucous tissue, leading to stricture of the urethra, together with epithelial and glandular changes.

Etiology.—The causes of chronic urethritis are—repeated attacks of gonorrhœa, the presence of a former stricture of the urethra which leads to retention of the secretions, abuse of alcoholic drinks, irritating or prolonged injections, granular patches in the urethra, folliculitis, prostatitis, etc. Some patients appear to be predisposed to chronic urethritis from the first without any apparent cause. Gout, scrofula, and tuberculosis are said to be predisposing causes. According to Guyon, the urethra is more liable to gonococcal infection after the first attack of gonorrhœa.

Morbid Anatomy.—In most cases the inflammation is localized to certain parts of the urethra—the anterior urethra, the bulb, or the membranous and prostatic portions. The morbid changes may be confined to the epithelium and glands of the mucous membrane, or may extend to the submucosa and spongy tissue.

The normal cylindrical epithelium of the urethral mucous membrane undergoes transformation into flat lamellar cells resembling those of the epidermis. This keratinization of the epithelium is an obstacle to the action of topical remedies. The subepithelial tissue becomes infiltrated with embryonic cells, and this infiltration may extend to the tissue of the corpus spongiosum and corpora cavernosa. This neoplastic cellular tissue is especially abundant around the lacunæ and follicles of the mucous membrane, and favours the stagnation of their secretions and the indefinite production of filaments in

the urine. It also gives rise to the development of the granular patches which are common in chronic gonorrhœa.

Later on the embryonic tissue becomes vascularized and organized into fibrous tissue. The lacunæ and glands, at first dilated, are filled with the newly formed connective tissue, and may become atrophied or transformed into cysts. The process of sclerosis may be confined to the lacunæ and glands, and give rise to localized thickenings of the mucous membrane; but in more severe cases it extends to the corpus spongiosum and corpus cavernosum, and leads to subsequent *stricture*. According to Guyon, stricture does not occur till four to eight years after the attack of urethritis which gave rise to the deep infiltration.

During this process of fibrous transformation the gonococci become attenuated and are difficult to find. On the occasion of acute exacerbations of the urethritis, however, they become more apparent, and are then found in the epithelial cells as well as in the leucocytes.

Symptoms.—The characteristic sign of chronic urethritis is the indefinite persistence of the 'morning drop' of discharge which glues together the lips of the meatus. This discharge consists of mucus, epithelial cells, and leucocytes, and contains gonococci. The symptoms are usually slight, but there may be some burning sensation along the urethra, and frequent desire to micturate. Acute exacerbations may supervene on the occasion of coitus, alcoholic excess, etc.

Chronic urethritis may be limited to the anterior urethra, but more often affects the posterior urethra, in which case the prostate is almost invariably affected, and frequently also the neck of the bladder. In fact, chronic posterior urethritis is almost synonymous with chronic prostatitis, and inflammation of the neck of the bladder never occurs without posterior urethritis (Guyon).

Diagnosis.—Examination of the *urine* should be made by the two-glass test. The urine of the first glass contains mucus and filaments, and, if the posterior urethra is affected, the second glass also contains filaments; if the anterior urethra only is affected, the second glass of urine is clear.

According to Finger, the appearance of the morning urine often shows the duration of the urethritis. If the urine is turbid, and contains much mucus, the urethritis is superficial and recent; if the morning urine is clear, containing only a few filaments and very little mucus, the urethritis is more localized and of older date.

The presence of *filaments* in the urine indicates inflammation of the urethral glands, and is of great importance in diagnosis. Muco-epithelial filaments composed of flat cells indicate that epithelial transformation has taken place in the mucous membrane, and that the lesion is one of long standing. Filaments from the prostatic ducts are usually convoluted or comma-shaped, and are formed of two layers of cylindrical cells. These prostatic filaments are expressed at the end of micturition, and are found in the last glass of urine; they prove the existence of posterior urethritis. The filaments should be examined for gonococci.

After gonococci have disappeared from the discharge and from the filaments a condition of *post-gonococcal microbial urethritis* may persist, which is due to infection by secondary microbes. Still later there may be a phase of *non-microbial urethritis*, in which no microbes can be found by microscopical examination.

Chronic urethritis must not be mistaken for *urethrorrhœa*, in which the discharge is clear and transparent, and comes from Cowper's glands.

Neisser's Method of Testing by Chemical or Mechanical Provocation.—In order to decide whether a patient is cured of gonorrhœa or still infectious, Neisser adopts the following procedure: The patient is requested to come for examination with the bladder as full as possible. Microscopical preparations are made from the anterior urethra, the posterior urethra, and the prostate. The secretion from the anterior urethra is obtained by squeezing the penis. The anterior urethra is then irrigated, by a thin catheter introduced as far as the sphincter, with 3 per cent. boric lotion. The patient then micturates, and any threads or flocculi in the posterior urethra will thereby be evacuated. The third step consists in massage

of the prostate and seminal vesicles, which expresses the secretion into the urethra. The patient then empties the bladder, and the urine contains the secretion expressed from the prostate and vesicles; in this way specimens are obtained from the anterior and posterior urethra and the prostate, and these are examined for gonococci by staining with methylene blue and decolorizing by Gram's method.

If no gonococci are found after this procedure, Neisser adopts the method of provoking irritation of the urethra to reveal them if present. The urethra is first irrigated with oxycyanide of mercury solution, to destroy the other bacteria which inhabit the urethra, and some hours afterwards a solution of protargol (3 to 5 per cent.), containing 5 per cent. of antipyrin, is injected into the anterior urethra. A purulent secretion appears the next morning, which is free from urethral bacteria. If no gonococci are found in this secretion the same procedure of irrigation and chemical provocation is repeated after two or three days; or, instead of this, mechanical irritation is exercised by means of a bulbous sound, the object of which is to express the gonococci from the urethral folds and follicles. The secretion thus obtained is carefully examined for gonococci.

If the examination for the gonococcus is still negative, and the secretion contains chiefly epithelial cells and mucus, Neisser is of opinion that probably no more gonococci are present. In cases of post-gonorrhœal urethritis, in which three or four provocations at intervals of several days, followed by two or three microscopical and cultural examinations of the urethral and prostatic secretions, show a negative result, he is satisfied that there is no risk of infection. If, on the other hand, the secretion shows an abundance of pus cells, and there is a tendency to exacerbations, gonococci are probably still present.

The value of this somewhat heroic method of investigation would therefore appear to be discounted by the fact that it is not always conclusive. Since a negative examination for gonococci does not prove that they are absent, it would seem better practice to trust to the simpler rule of examining the

discharge for pus cells and filaments, and to regard every patient as possibly infectious in whom they are found.

Moreover, this violent manipulation of the urethra is open to several objections. In the first place, it cannot be free from the risk of setting up general gonococcal infection by liberating the gonococci and opening up new channels of infection through breaches of surface in the mucous membrane caused by the instrument; in the second place, it may retard the patient's ultimate recovery.

Prognosis.—The prognosis of chronic gonorrhœal urethritis is grave, owing to the possibility of *stricture*, and the occurrence of complications which may supervene at any period of the disease. The discharge and filaments remain contagious for long periods, and are the cause of numerous contaminations of married women by husbands who think themselves cured. However, simple non-infectious muco-epithelial filaments may be found in the urine some years after the gonorrhœa is cured. These are also said to occur in persons who have never had gonorrhœa; but this statement must be received with reserve, for, as Ricord remarked, 'there are few who escape it.'

In nervous subjects chronic gonorrhœa may lead to sexual neurasthenia, manifested by frequent emissions and hyperæsthesia of the genital organs, or by loss of power of erection, and consequent mental depression and general debility. These symptoms occur especially in cases of posterior urethritis, but only in certain subjects. It is therefore necessary to take into account the temperament of the patient in formulating a prognosis.

In chronic urethritis the gonococcus may sometimes reappear on the occasion of acute exacerbations, which are apparently spontaneous, but really due to follicular or prostatic lesions which have been irritated by excess of coitus, etc. These acute exacerbations of latent gonorrhœa are often attributed by the patient to a fresh infection.

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CHAPTER XXIII

TREATMENT OF GONORRHŒA IN THE MALE

Acute Urethritis.

DURING the acute stage the patient should be kept quiet indoors if possible. The diet should be simple, and all alcoholic drinks should be avoided. Large quantities of fluid should be drunk in the form of lemonade, barley-water, or infusion of *buchu* or *uva ursi*. Warm baths are soothing, but should be total, as simple immersion of the parts in a hip-bath provokes congestion. Cold compresses may be applied to the penis if there is pain and œdema, and an ordinary small sponge bag containing absorbent wood-wool, and perforated for ventilation, may be worn to collect the discharge. The testicles should be supported by means of bathing-drawers—a more efficacious method than the usual suspensory apparatus. The bowels should be kept open by saline aperients. A pill containing $\frac{1}{4}$ grain of opium, 3 grains of camphor, and $\frac{1}{4}$ grain extract of belladonna should be given at bedtime to prevent painful erections during the night. If there is much chordee, morphia suppositories may be used.

The patient should be informed of the contagious nature of the discharge, and of the danger of conveying it to the eye by his fingers.

Internal Medication.—The balsams, *copaiba*, *cubebs*, and *santal oil*, should not be given in the acute stage, but should be reserved for the *period of decline*. Balzer recommends a mixture of salicylate of soda 30 grains and bicarbonate of soda 60 grains taken in lemonade at intervals during the day. Salol in 10-grain doses thrice daily is also useful, and some recommend urotropin, aspirin, and helmitol.

When the acute period has subsided, balsams may be given. *Copaiba* may be administered in capsules, either in the form of balsam or resin, in doses of 1 drachm daily. *Cubebs* (oleo-resin) and *santal oil* may be given in daily doses of ½ to 1 drachm, in capsules. A new preparation of santal, known as *santalol B*, is said to be better tolerated than the usual santal oil; this is given in capsules of 4 grains, to the amount of 15 to 30 grains daily. Balzer recommends a mixture of copaiba, cubebs, salicylate of soda, and subcarbonate of iron.

One of the latest preparations is *gonosan*, a mixture of santal oil (80 per cent.) and kava-kava (20 per cent.). Kava is a tonic astringent resin obtained from the roots of *Piper methysticum*. Gonosan is said to be both analgesic and anaphrodisiac. According to Schindler and Siebert gonosan has no bactericidal action on the gonococci, whether given internally or applied locally.

The important point in the administration of balsams for acute gonorrhœa is not to give them too soon, and to continue them in progressively diminished doses till all symptoms have disappeared. They sometimes cause gastro-intestinal disturbance, and should therefore be taken after meals. Copaiba sometimes causes an erythematous rash on the limbs and trunk, but the injurious effect of balsams on the kidneys has probably been exaggerated. The action of the balsams is due to a tonic astringent action on the mucous membrane of the urethra during excretion by the urine.

Local Treatment.—The local treatment of acute urethritis may be carried out either by injections or by irrigation of the urethra by hydrostatic pressure. As the object of this treatment is to destroy the gonococci as far as possible by bactericidal substances, it is obvious that local treatment should be commenced as soon as possible. However, as there is much difficulty in carrying it out during the presence of acute and painful symptoms, and also a danger of lacerating the swollen and tender urethral mucous membrane, it is best to wait till the acutely painful period has subsided before commencing local treatment of the urethra. In subacute cases of gonorrhœa, in which these acute symptoms are absent, local treatment may be commenced at once.

Abortive Treatment. — Some authors advocate an abortive treatment of gonorrhœa by commencing local treatment of the urethra at the onset of the disease. There must, of course, be a time when an abortive cure is possible, but this time is limited to the first few hours after infection, during which time the patient seldom presents himself for treatment. As a rule, a patient has been infected for two or three days before he seeks advice, and abortive treatment is then unlikely to succeed. On the other hand, as Finger points out, the ordinary treatment of gonorrhœa may sometimes result in aborting the disease if the case is seen early.

Neisser and Jadassohn are not in favour of the abortive method, and the latter authority states that gonococci often reappear about ten days after so-called abortive cures.

There appears, therefore, to be a consensus of opinion among the leading authorities, including Neisser, Finger, and Jadassohn, that the so-called abortive treatment of gonorrhœa is unreliable and usually inefficacious, and that local urethral medications should be commenced only after the acute symptoms of the first two or three days have subsided. Moreover, injections during the acute period have been said to cause prostatitis and epididymitis.

Urethral Injections.—Before treatment by injections is commenced the urine should be examined by the two-glass test to determine if the posterior urethra is affected. If the *anterior urethra* only is found to be affected, the injections may be confined to this, and can be carried out by the patient himself. In most cases, however, the posterior urethra is affected during the second or third week of the disease.

The syringe should have a short conical nozzle, so as to plug the meatus, and a capacity of 10 to 15 c.c. (½ ounce). After passing water to clear the urethra, the meatus and fossa navicularis are first cleansed, without introducing the nozzle of the syringe sufficiently to close the meatus. The anterior urethra may then be injected either with the meatus closed or open—(1) in the former case the patient closes the meatus by pressing with his fingers against the nozzle of the syringe, and retains the injected fluid for five to ten minutes;

(2) in the open method the procedure consists in irrigation of the anterior urethra by means of the syringe. The open method of syringing is the best if the disease is confined to the anterior urethra, because with a closed meatus the injection may easily reach the posterior urethra, and possibly infect it by driving back the secretion. It is therefore best to begin with this method in the early stages of acute gonorrhœa, although, as previously mentioned, the posterior urethra will require subsequent treatment in the majority of cases.

If the *posterior urethra* is affected, there are three methods of treatment — (1) deep injections by means of an ordinary syringe; (2) irrigation of the whole urethra by means of a syringe and catheter; (3) irrigation without a catheter (Janet's method).

Injections.—Some authorities have stated that injections with an ordinary syringe do not reach the membranous and prostatic parts of the urethra; but Vajda demonstrated some time ago, by injecting a solution of methylene blue and afterwards examining with the urethroscope, that this view was incorrect, and that injections with an ordinary syringe can be made to reach the posterior urethra. About 3 drachms of fluid are enough to reach the posterior urethra.

Irrigation with Syringe and Catheter.—For this purpose a thin, flexible gum catheter is used, fixed to a larger syringe than that used for ordinary injections. After preliminary irrigation of the anterior urethra, the catheter is passed into the bladder and withdrawn till no urine passes; it is then in the posterior urethra. The syringe is then attached, and a small quantity of fluid injected. If this returns by the meatus, the end of the catheter is not beyond the sphincter and must be readjusted. If no fluid returns either by the meatus or by the catheter, the latter is in its proper position. A series of successive injections is then made, so as to 'gargle' the posterior urethra. After this the catheter is gradually withdrawn, keeping up the injection all the time, so as to treat the whole urethra from behind forwards.

Irrigation without Catheter.—By this method, which is known as Janet's, the whole urethra and bladder are irrigated by

hydrostatic pressure. The apparatus consists of a glass vessel holding about 3 or 4 pints, a rubber tube and siphon, and a glass cannula with a blunt conical nozzle and small perforation. The pressure is regulated by raising the glass vessel by means of a pulley or some other mechanism. The patient should be in the recumbent position, and the fluid should be warmed to 38° C. The glans penis and prepuce are first washed with 1 in 2,000 perchloride of mercury. The anterior urethra is then irrigated with the meatus open, by means of the apparatus raised sufficiently for the liquid to flow through the tube. The glass vessel is then raised to the height of about 5 feet, which is sufficient to obtain enough hydrostatic pressure for the fluid to overcome the resistance of the sphincter muscle and enter the bladder. The nozzle of the glass cannula is then fixed in the meatus, and the glans penis held against it with the fingers of the left hand, the right hand being used to regulate the flow of fluid. When the irrigator tube and cannula are first filled, an air bubble should be left in the cannula to serve as an index to the rate of flow by its oscillations. The patient is told to relax the sphincter vesicæ by attempting to urinate, and at this moment the fluid is allowed to pass into the bladder. This should be done with the least possible pressure, and should cause no pain if properly performed. If spasm of the membranous part of the urethra occurs, the flow should be temporarily interrupted, and continued when the spasm has ceased. When the operation is complete, the patient passes water, including the fluid passed into the bladder. By the hydrostatic pressure the folds of the urethra are distended, and the whole mucous membrane is brought under the action of the fluid.

The irrigation method was originally introduced by Janet for the abortive treatment of gonorrhœa, and was commenced on the first day with irrigations of permanganate of potash, which was used in gradually increasing strengths from 1 in 4,000 to 1 in 500. However, as the abortive treatment of gonorrhœa is known to frequently fail, and as the technique of the method is difficult to carry out in private practice, the method of irrigation by hydrostatic pressure cannot be said to fulfil the promises that were claimed for it.

Guiard and others prefer irrigation by means of a syringe, as this gives more control over the performance. With hydrostatic pressure the operation cannot be regulated with the same nicety as with a syringe, and there is danger of over-distending the bladder and giving rise to painful tenesmus, or even cystitis.

Solutions for Injection and Irrigation.—The number of therapeutic agents which have been recommended for the local treatment of urethral gonorrhœa is legion, and a list of the most important is given in the Appendix. For practical purposes they may be divided into two classes—(1) bactericidal agents, which destroy the gonococci; (2) astringents, which restore the tone of the urethral mucous membrane.

The chief bactericidal agents are perchloride of mercury, oxycyanide of mercury, ichthyol, nitrate of silver, permanganate of potassium, and chloride of zinc. The chief astringent preparations are the sulphates of zinc and copper, acetate of zinc and lead, alum, tannin, bismuth, etc.

According to Neisser, the *silver salts* are the most active in destroying gonococci, and of late years a number of new silver preparations have been manufactured to replace silver nitrate. The more important of these are protargol, argonin, argentamine, largin, actol, itrol, ichthargan, and albargin. Itrol is a citrate of silver, actol a lactate of silver, and the others combinations of silver with an albuminous basis. The advantages claimed for these drugs are—(1) absence of irritation; (2) greater penetrative power; (3) a stronger bactericidal action on the gonococci; (4) absence of the coagulative action on albumin, which limits the action of silver nitrate. Protargol is recommended by Neisser, who introduced it, in the strength of ¼ to 1 per cent. Jadassohn advocates ichthargan and albargin; Finger prefers protargol or argonin.

The bactericidal power of the new silver salts has recently been investigated by Marshall and Neave. Their results are—(1) That actol, itrol, argentamine, argentol, albargin, argonin, ichthargan, largin, novargan, and protargol have a powerful bactericidal action, equivalent to that of silver nitrate or silver fluoride; (2) that nargol has much less action; (3) that collargol and argyrol have no bactericidal action; (4) that the

percentage of silver in the compounds is no criterion of the bactericidal power (see Appendix). Unfortunately, these experiments were carried out on the *Staphylococcus pyogenes*, and not on the gonococcus. However, they support the value of the new silver compounds, with the exception of argyrol, nargol, and collargol.

Conclusion.—Taking all the evidence into consideration, it appears that the best routine treatment for acute gonorrhœal urethritis is as follows:

1. During the acute stage—that is, during the first two or three days—both local treatment and internal administration of balsams should be avoided, and the patient treated simply by antiphlogistic measures.

2. As soon as possible injection or irrigation should be commenced, limited at first to the anterior urethra if the posterior urethra is found by the two-glass test to be unaffected.

(*a*) If injections are used, a $\frac{1}{4}$ per cent. solution of protargol (or one of the other silver preparations) should be injected three or four times a day, and retained by closing the meatus for five to ten minutes.

(*b*) If irrigation is used, the same solution should be injected by means of a small catheter passed to the bulb of the urethra, the meatus being left open.

The former method has the advantage that the patient can perform it himself. In either case the strength of the solution should be gradually increased to 1 per cent.

3. During the second week balsams may be administered—santal oil, cubebs, copaiba oil or resin, in capsules of 10 minims; or gonosan capsules, thrice daily after meals.

4. This treatment should be continued for at least four weeks, after which astringent injections of chloride ($\frac{1}{2}$ to 1 grain to 1 ounce), sulphate or acetate of zinc (2 to 4 grains to 1 ounce), or some other astringent drug, should be continued two or three times a day till the discharge has ceased and the gonococci or filaments have disappeared. It is a mistake to continue the astringent injections for months on end, as is done by some patients, as a persistent catarrh of the urethral mucous membrane is often produced by this practice.

5. If the posterior urethra becomes affected during the course of the attack (according to Balzer and Guiard this happens in most cases), the injections must be made to reach the posterior urethra, and this can be done by steady pressure with an ordinary urethral syringe with the meatus closed. The surgeon may also practise irrigation of the posterior urethra every other day by means of the syringe and catheter.

As regards the *duration* of the attack, an abortive cure, as previously pointed out, cannot be relied upon, either by Janet's irrigation method or by the use of the new preparations of silver, etc., and in the opinion of Finger the duration of acute gonorrhœa in the male still remains on the average of six to eight weeks' duration, although the complications may be less frequent than formerly. Some cases recover without local treatment of the urethra, but this cannot be depended upon.

Prophylaxis.—Certain injections practised immediately after coitus have been recommended as a prophylactic measure against gonorrhœal infection. The chief of these are nitrate of silver, 2 per cent.; protargol, 4 per cent.; and perchloride of mercury, 1 in 4,000. The introduction of 10 per cent. protargol ointment into the meatus has also been advocated. These measures are, however, of doubtful value; for, in the first place, it is difficult to carry them out sufficiently early to be efficacious, and in the second place they may cause irritation of the urethra, and open up the surface to the very infection which it has been wished to avoid. Finger states that the regular use of these preventive measures may give rise to a chronic catarrh, with epithelial degenerations of the mucous membrane, which is as bad as gonorrhœa itself, and also predisposes the urethra to gonorrhœal infection. Guyon mentions a fatal case in a man who developed diffuse phlegmonous prostatitis after practising forcible prophylactic injections.

Chronic Urethritis.

General treatment consists in the avoidance of excesses of all kinds, and the adoption of a simple but nutritious diet. Alcoholic drinks are best avoided, but there is no harm in

taking a moderate quantity of claret with meals, as this in itself has a slight astringent action. Salol or the salicylates should be given internally in 10 to 15 grain doses thrice daily after meals. There does not appear to be much advantage in continuing the use of the balsams, as they are apt to cause digestive disturbance when used for long periods.

If the urethritis is superficial, and limited to the *anterior urethra*, a rapid cure can often be obtained by irrigation with permanganate of potash (1 in 4,000) or protargol (1 in 1,000). After gonococci have disappeared from the discharge, Balzer recommends irrigations with perchloride of mercury (1 in 20,000) or oxycyanide of mercury (1 in 4,000), to neutralize secondary infection of the urethra. The mercurial salts are especially indicated in secondary infection associated with the gonococcus. When the discharge appears to be amicrobial-astringent injections are indicated, especially the salts of zinc. Ultzmann employs a mixture of carbolic acid, sulphate of zinc, and alum, ½ grain of each to 1 ounce of distilled water. Janet recommends a combination of permanganate of potash (1 in 3,000) and perchloride of mercury (1 in 20,000).

When the *posterior urethra* is affected, or when there are localized foci of chronic inflammation to deal with, recourse must be had to other methods of local treatment. These include instillations, dilatation, and local applications through the urethroscope.

Instillation.—The object of instillation is to slowly inject drop by drop a strong solution into a certain limited part of the urethra. This method allows the use of stronger solutions than can be used for injection or irrigation, and is especially indicated in circumscribed inflammatory lesions. The procedure advocated by Guyon, who introduced the method, is as follows:

Guyon's apparatus consists of a graduated syringe, holding 4 c.c., the piston of which can be worked either with a screw or in the ordinary way. The syringe fits tightly into a thin olive-headed gum catheter, finely perforated at the end. This, being flexible, is preferable to the metal catheter which is used in Ultzmann's syringe for the same purpose. The

cannula of the syringe is pointed to fit into the catheter, but its lumen is cylindrical, and of the same diameter as the lumen of the catheter, so as to insure uniform pressure. The catheter is rendered aseptic before use by syringing it with carbolic lotion, as it cannot be boiled like a metal instrument. The liquid in the syringe is expressed drop by drop by a screw motion of the piston during the process of instillation.

Previous to the operation the patient passes water; the urethra is irrigated with boric lotion, and afterwards cleaned and dried by means of wool tampons passed by a pair of long urethral forceps. This precaution prevents contamination of the posterior urethra by matter pushed backwards from the anterior urethra by the passage of the instillator.

1. *Instillation of the Posterior Urethra.*—A little boiled water or boric acid should first be injected into the bladder. The olivary instillator is then passed beyond the sphincter muscle. By gently withdrawing it the end can be felt to be beyond the sphincter and placed in the posterior urethra. About 20 to 40 drops of solution are then passed very slowly. The posterior urethra has no reservoir, like the bulb of the anterior urethra, so that the instilled fluid soon enters the bladder, and its effect on the posterior urethra is transient. For this reason more fluid is required in instilling the posterior than the anterior urethra, and the bladder should contain some fluid to dilute the solution which passes into it from the posterior urethra.

2. For the *anterior urethra* a larger olive-headed instillator is required, in order to prevent return of the fluid and localize it to the part to be treated. After instillation of a few drops of fluid the instrument should be kept in place for one or two minutes.

3. When instillation is required for *both the anterior and posterior urethra*, the latter should be treated first, after injecting some boric acid solution or boiled water into the bladder. After instilling about 20 drops into the posterior urethra, the instrument is slowly withdrawn, leaving a few drops of solution in its passage, and about 10 drops instilled into the anterior urethra.

4. When instillation is required for *cystitis of the neck of the*

bladder, the same method of procedure is used as for the posterior urethra, except that the bladder must be previously emptied and the instillation should be more rapidly performed. It is necessary in these cases to treat the posterior urethra as well, because 'every cystitis is accompanied by posterior urethritis' (Guyon).

Solutions for Instillation.—The solutions used by Guyon are *silver nitrate*, 1 to 5 per cent.; *perchloride of mercury*, 1 in 5,000 to 1 in 3,000; *copper sulphate*, 5 to 8 per cent. *Protargol*, 2 to 5 per cent., is more easily supported by the patient than nitrate of silver.

Retained Injections.—Motz advocates injection of the urethra with solutions which are retained for upwards of an hour by tying a gauze bandage round the meatus. The applications are made every day or every other day, and are preceded by irrigation of the urethra with 1 in 2,000 oxycyanide of mercury. The solution used by Motz for this purpose consists of hermophenyl and protargol, $\frac{1}{4}$ to $\frac{1}{2}$ grain; glycerine, 15 minims; cocaine, $\frac{1}{2}$ grain; distilled water, 1 ounce. The glycerine softens the keratinized epithelium; the protargol is said to cause slight diapedesis towards the epithelium, and facilitates the penetration of the mercurial salt.

In cases of *posterior urethritis* Motz recommends massage of the prostate, followed by rectal suppositories of mercurial ointment and instillation of the posterior urethra with silver nitrate (1 per cent.).

Treatment by Ointments and Bougies.—Tommasoli advocates the injection of ointments containing nitrate of silver, sulphate of copper, protargol, sulphate of zinc, iodoform, etc., by means of a special syringe. Casper uses similar ointments, applied by means of a grooved sound. Berkeley Hill used theobroma bougies containing chloride or sulphate of zinc with opium and belladonna; these were inserted at bedtime and dissolved during the night. Other surgeons have used iodoform bougies of a similar nature, and more recently gelatin has been used as the basis for medicated urethral bougies. None of these methods appear, however, to be as satisfactory as the instillation or injection of aqueous solutions.

Dilatation.—In cases of commencing stricture, or patches of local infiltration of the mucous membrane, dilatation of the urethra by means of a sound is indicated. These should be retained for fifteen to twenty minutes, and may be lubricated with ointment containing silver nitrate, protargol, etc. The sound, by dilatation of the urethra, favours the absorption of submucous inflammatory infiltrations, and expresses the contents of the inflamed lacunæ and glands of Littré. This action is assisted by gentle massage of the affected parts of the urethra on the sound. A large-sized metallic sound (No. 10 or 12, English) should be passed every two or three days, for a few days, and each dilatation should be followed by irrigation with oxycyanide of mercury (1 in 4,000). After the first operation the sound is withdrawn covered with pus, but this becomes gradually less abundant after each successive dilatation. The combined method of dilatation and massage of the urethra may be supplemented on each occasion by prolonged injection of the urethra by Motz's method, mentioned above.

Urethroscopy.

The urethroscope has during recent years been extensively used for the diagnosis and treatment of urethral lesions, and when reserved for proper cases is a useful instrument. On the other hand, the indiscriminate use of the urethroscope for purposes of diagnosis is to be severely condemned, and it is probable that the *abuse* of this instrument has sometimes led to complications in cases of urethritis which might not have occurred without it.

As Taylor well remarks, 'it is an instrument of reserve rather than of routine, and it should always be used in a rational and conservative manner. It is to be regretted that it has been used very much as a toy, and has been to some simply a surgical hobby.'

It may therefore be laid down as a rule that the urethroscope should *never be used in acute or recent cases of urethritis*. It is especially indicated for *simultaneous diagnosis and treatment*, and should not be passed an unnecessary number of times for purposes of diagnosis only.

PLATE V.

URETHROSCOPIC EXAMINATION OF THE URETHRA. (AFTER LUYS.)

FIG. 1.—NORMAL URETHRA, SHOWING LONGITUDINAL FOLDS.

FIG. 2.—NORMAL URETHRA, SHOWING LARGE LACUNA OF MORGAGNI.

FIG. 3. — INFLAMED LACUNÆ OF MORGAGNI.

FIG. 4. — INFLAMED AND CYSTIC GLANDS OF LITTRÉ.

FIG. 5.—INFILTRATION OF MUCOUS *MEMBRANE*.

FIG. 6.—STRICTURE OF URETHRA.

The great *advantage* of urethroscopic treatment over Guyon's method of deep instillation is that the diseased area can be seen, and the medicament applied directly to it; while in the method of instillation there is the objection of working in the dark, and also the spreading of concentrated lotions to the healthy areas of the mucous membrane. Again, by the urethroscope different forms of treatment can be applied to different areas at the same time. On the other hand, it is easier to perform Guyon's instillation than to apply solutions to the posterior urethra through the urethroscope, as the latter performance requires much practice.

Technique.—There are two forms of urethroscope, one of which acts by reflected light, the other by direct illumination. In the latter a small electric lamp is passed down the tube. The advantage of the latter form is that it gives more light; the disadvantages are, less room for manipulation, and the possibility of the lamp getting broken off.

Before urethroscopic examination it is better for the patient not to pass water for an hour or two. The glans penis and meatus should be cleaned with perchloride of mercury lotion (1 in 2,000), and the tube should be lubricated with *glycerine*, Cocaine or stovaine may be necessary in some cases. In cases of narrow meatus it may be necessary to enlarge the orifice before the tube can be passed.

The patient should lie on the operating-table with his legs hanging over the end, and the feet supported on rests. For examination of the anterior urethra the penis may be held vertically, but must be depressed to the horizontal position for examination of the posterior urethra.

Contra-indications.—The urethroscope should never be used in acute or recent cases of urethritis, or in cases of acute prostatitis or epididymitis. It should be reserved for cases of chronic urethritis and gleet in which there is no pain on micturition or erection, and in which the urine is comparatively clear.

The Normal Urethra.—The red colour of the normal urethra varies in different subjects, and also with the degree of pressure of the tube. The longitudinal folds of the urethra

appear as radiating furrows in the circular image seen through the urethroscope (Fig. 1, Plate V.). The epithelium is normally smooth and shiny, but becomes rough and dull when diseased. The lacunæ of Morgagni appear as **V**-shaped depressions on the dorsal surface of the urethra (Fig. 2, Plate V.). The glands of Littré are hardly visible in the normal urethra. The verumontanum appears as a fusiform swelling in the floor of the urethra, but the prostatic sinuses and ejaculatory ducts are not easily seen unless they are diseased and discharging pus.

The Pathological Urethra.—The chief conditions visible by the urethroscope in cases of chronic urethritis are—

1. *Soft infiltration*, in which the urethra is dark red and swollen in parts, the longitudinal striation obliterated, and the surface dull or rough (Fig. 5, Plate V.).

2. *Hard infiltration*, the beginning of stricture, in which the mucous membrane is hard and parchmenty, and of a pale yellowish-gray colour (Fig. 6, Plate V.).

Hard infiltration occurs especially in the middle of the penile urethra, the bulb, and the membranous urethra—the three usual seats of stricture.

Patches of soft and hard infiltration may alternate in the same urethra, and also alternate with areas of healthy mucous membrane.

3. *Inflamed glands of Morgagni* (Fig. 3, Plate V.).

4. *Inflamed and cystic glands of Littrê* (Fig. 4, Plate V.), which may be either inflamed and discharging pus, or cystic from obliteration of their ducts.

5. *Papillomata and polypi.*

6. Discharge of pus from the *prostatic sinuses* and ejaculatory ducts.

7. *Granular patches* in the mucous membrane.

Urethroscopic Treatment.—The principal methods of treatment which may be applied through the urethroscope are—(1) the application of caustics, (2) electrolysis of the inflamed glands and lacunæ, (3) galvano-cautery, (4) internal urethrotomy.

The urethra should be previously irrigated with oxycyanide of mercury (1 in 4,000) or some other antiseptic.

APPLICATION OF CAUSTICS.—This consists in the cauterization of chronically inflamed patches of mucous membrane with silver nitrate. Luys prefers the solid caustic, which is applied on the end of a fine probe. The applications should be made to the deepest parts first. Silver nitrate solution may be applied to the posterior urethra through the urethroscope, instead of using Guyon's instillation syringe.

Another useful application is tincture of iodine applied on a wool tampon, passed by a pair of long urethral forceps.

ELECTROLYSIS.—This is especially indicated in chronic inflammation of the glands of Littré and lacunæ of Morgagni. A fine platinum point connected with the negative pole is passed down the tube, and inserted into the glandular orifice, the positive pole being placed on the patient's body. A current of 2 to 5 milliampères destroys the glands in a few minutes. This method is identical with that for the electrolysis of hairs.

GALVANO-CAUTERY.—This is indicated for the destruction of polypi and papillomatous proliferations, and also in cases of chronic suppuration in the larger lacunæ of Morgagni. After drying the mucous membrane with wool tampons the cautery is passed cold, and the current is turned on when the desired point is touched.

INTERNAL URETHROTOMY.—This may be used for the incision of periurethral abscesses or for the division of stricture. The internal incision of a periurethral abscess avoids the formation of a urethral fistula.

Oberlaender has devised special fine-bladed urethrotomes for the scarification or incision of hard infiltration of the urethra.

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CHAPTER XXIV

COMPLICATIONS OF GONORRHŒA IN THE MALE

GONORRHŒAL URETHRITIS may be complicated locally by balanitis, œdema, and lymphangitis; or the inflammatory process may extend to the glands of the urethra, the prostate, Cowper's glands, the vesiculæ seminales, vas deferens and epididymis, and the bladder.

Balanitis.—This seldom occurs except in persons with a long prepuce, which causes retention of discharge, and consequent inflammation of the glans and prepuce. Œdema of the prepuce, lymphangitis with bubo, phimosis and fissures of the preputial orifice, may result; and in severe cases there may be sloughing of the prepuce. Paraphimosis is liable to occur if the œdematous prepuce is drawn back.

Treatment.—Prolonged local boracic baths; elevation of the penis; irrigation with 1 in 1,000 solution of perchloride of mercury by means of a soft catheter inserted within the prepuce. If adhesions are left after the inflammation has subsided, circumcision may be advisable.

Cowperitis.—Inflammation of the glands of Cowper, which are situated one on each side of the membranous urethra, may lead to circumscribed or diffuse abscess with infiltration of urine. Cowperitis is generally unilateral, and forms a round, painful swelling which can be felt on one side of the perineum. If an abscess forms, it generally points on the perineum; it rarely opens into the urethra or rectum. Infiltration of urine is rare, but urinary fistula may possibly occur. In some cases Cowperitis pursues a chronic course, with a mucous discharge which may persist long after the urethritis has subsided.

Periurethritis.—In some cases the gonorrhœal inflamma-

tion may extend to the corpus spongiosum, causing painful erections; or it may reach the corpus cavernosum, causing cavernitis. Acute periurethritis sometimes follows the use of violent or irritating injections, or the injudicious use of catheters and sounds. *Cavernitis* forms a painful fusiform swelling in the perineum. Resolution is the rule, but suppuration may occur, or sclerosis, causing trouble in erection.

Prostatitis.—Gonorrhœal inflammation may affect the prostate in the form of acute prostatitis, chronic prostatitis, or catarrhal prostatitis. The last form affects the prostatic glands, and is usually associated with posterior urethritis. According to Finger, prostatitis plays a considerable rôle in the evolution of gonorrhœa.

Acute Prostatitis.—This generally appears in the second or third week, sometimes as the result of irritating or forcible injections.

The *symptoms* consist in perineal discomfort and pain at the end of micturition. As the inflammation increases, the pain becomes more acute and radiates to the rectum and lumbar region. Micturition becomes frequent and painful, and there is sometimes retention of urine. Sometimes there is blood mixed with the urine at the end of micturition. Defæcation also becomes painful, and the prostate gland is tender to rectal palpation. If suppuration occurs, there is a rise of temperature, accompanied by rigors and other febrile symptoms.

Acute prostatitis may end—(1) in resolution, in the course of one or two weeks; (2) in suppuration; (3) in chronic prostatitis. When suppuration occurs, the abscess may open into the urethra, bladder, or rectum, causing instant relief to the acute symptoms. It may, however, open into the cellular tissue, forming a periprostatic abscess, which is liable to infiltration with urine. This form of termination is unfavourable, and may result in chronic fistula.

Opening of the abscess into the urethra is the most usual occurrence, and in this case pus is evacuated during micturition, or accumulates behind the sphincter urethræ, and is expelled by ejaculation. Evacuation by the urethra is generally followed by healing in three or four weeks.

CATARRHAL PROSTATITIS.—This is the most common form, and occurs with posterior urethritis. The symptoms consist in more or less trouble and frequency in micturition; occasionally there is retention of urine. The urine contains *prostatic filaments*, which are important in diagnosis. When the patient is made to pass urine into two glasses, the second glass, containing the prostatic filaments, shows the presence of catarrhal prostatitis, the first glass of urine being clear. Other symptoms include a certain degree of weight and discomfort in the perineum, pain on defæcation, and painful erections. According to Finger, there may be hæmorrhagic ejaculations, even in the absence of spermato-cystitis.

CHRONIC PROSTATITIS.—This may be a chronic form of the last associated with chronic posterior urethritis, or it may consist in chronic parenchymatous prostatitis with interstitial induration.

In chronic catarrhal prostatitis there is a mucoid discharge, which occurs on micturition or defæcation, sometimes in the form of a muco-purulent plug, which is evacuated by a more or less painful spasm at the end of micturition. If gonococci are still present, urethral reinfection may occur suddenly. A certain number of patients become neurasthenic and present certain nervous disorders, which only improve with treatment of the local condition. On the other hand, chronic prostatitis is likely to lead to a state of hypochondriasis.

Rectal examination shows the prostate to be slightly enlarged. By pressure a whitish fluid can be expressed from the urethra containing epithelial cells, leucocytes, fatty granules, and sometimes gonococci. These microbes may remain for a long time concealed in the more or less disorganized prostatic glands, and are a constant source of urethral reinfection. By making the patient urinate into three glasses, the third glass will contain the products of prostatic excretion. This excretion often occurs during defæcation. There is rarely much trouble with micturition in chronic prostatitis, but erection and ejaculation may be painful, especially in neurasthenic subjects.

The *prognosis* in chronic prostatitis in uncomplicated cases is

generally good, but a muco-purulent discharge may persist for a long time. When prostatitis has existed for some time it may cause permanent interstitial fibroid thickening, and finally *prostatic hypertrophy*.

Diagnosis.—The discharge from chronic prostatitis is distinguished from *spermatorrhœa* by the absence of spermatozoa. In tubercle of the prostate the gland is indurated in some parts and softened in others, and is less painful. Moreover, tubercle of the prostate is generally associated with tubercle of the epididymis, vesiculæ, and spermatic cord.

Treatment.—In *acute prostatitis* treatment includes rest in bed, hot baths, laxatives, and suppositories of opium and belladonna. Local treatment of the urethra must be suspended, and no catheter should be passed unless retention of urine fails to yield to other methods of treatment, such as the hot bath and opium. When suppuration occurs, a perineal incision should be made as soon as possible.

In *chronic prostatitis* the posterior urethra may be treated by combined dilatation and irrigation, or else by means of instillations of nitrate of silver or protargol by means of a Guyon's syringe. By some authors digital *massage of the prostate* is recommended as a preliminary proceeding to irrigation or instillation. Irrigation may be performed with permanganate of potash (1 in 2,000) or ichthyol (1 in 1,000); instillation by 2 to 5 per cent. protargol or 1 per cent. silver nitrate solution.

Some authors recommend electrolysis, the negative pole being in the rectum and the positive in the prostatic urethra. This proceeding is, however, of doubtful value, and any method requiring the repeated and prolonged passage of instruments is to be condemned. Hydrotherapy, sea-bathing, and cold douches are useful, combined with general hygienic treatment. Suppositories of mercurial ointment are recommended by some authorities. Internally, salol in 10-grain doses thrice daily is useful.

The treatment of prostatic gonorrhœa is beset with many difficulties. On the one hand, we know that gonococcal foci in the prostate may cause reinfection of the urethra, and even in some cases set up gonorrhœal pyæmia: on the other hand,

excessive instrumentation may light up latent foci, and cause the very complications it is wished to avoid. It is not improbable that the indiscriminate use of the urethroscope has been responsible for many cases of epididymitis, or even general gonorrhœal infection. Again, it is difficult to conceive how any amount of instillation or irrigation can affect foci of inflammation hidden away in the prostatic glands. Sir Henry Thompson long ago taught that 'the introduction of an instrument is, more or less, an evil, never to be resorted to unless a greater evil be present, which its employment may possibly remedy.' It is sometimes the best course to let sleeping dogs lie.

Cystitis.—Gonorrhœal cystitis is usually limited to the neck of the bladder or the region of the trigone, and is caused by direct extension from a posterior urethritis (urethro-cystitis). Sometimes there is a mixed infection by gonococci and pyogenic organisms affecting the whole bladder. Cystitis may occur in the third or fourth week of gonorrhœa, or later on as a complication of chronic urethritis. All causes which aggravate gonorrhœa, such as violent exercise, strong or forcible injections, catheterism, alcoholic drinks, etc., may provoke cystitis.

The *symptoms* consist in frequent desire to micturate, tenesmus, hæmaturia at the end of micturition, pain in the perineum, and along the urethra to the glans penis. The urine at the end of micturition contains pus, blood, and pyogenic organisms, sometimes gonococci. Retention of urine may be caused by spasm, or there may be incontinence.

Cystitis may undergo resolution in a few days or may become chronic, with a tendency to recurrences which may persist for years. In predisposed subjects gonorrhœal cystitis may lead to tuberculosis of the bladder.

Treatment.—This requires rest in bed, milk diet, hot baths, and avoidance of alcoholic drinks. All urethral injections should be stopped. Suppositories of opium and belladonna relieve the pain and tenesmus. Internally, buchu, salol, salicylate of soda, benzoate of soda, or capsules of terebinth may be tried. Bromide of camphor is also useful if there is much pain and dysuria.

Guyon recommends instillations of nitrate of silver (2 per cent.) every other day, or perchloride of mercury (1 in 5,000 to 1 in 1,000). Protargol (5 per cent.) may be substituted for nitrate of silver. Others advise irrigation of the bladder with permanganate. Treatment should be continued for some time after apparent cure, owing to the liability to relapse.

Cysto-pyelo-nephritis.—In rare cases gonorrhœa is a cause of pyelo-nephritis, generally due to pyogenic organisms complicating cystitis. However, cases have been reported in which pyelo-nephritis was caused by gonococci without previous cystitis.

The *symptoms* of pyelo-nephritis consist in fever and rigors, pain on pressure over the kidney, and pyuria. The urine contains pus, renal epithelial cells, and hyaline, epithelial and granular casts. Treatment is the same as for cystitis.

Deferentitis.—Gonorrhœal inflammation during the second week of the disease often extends from the posterior urethra along the vas deferens to the vesiculæ and epididymis. The *deferentitis* may be partial, and limited to the inguinal canal. It may be latent without objective symptoms, or may manifest itself by painful swelling and induration. The inflammation may extend to the other elements of the spermatic cord, constituting *funiculitis*. In this case the cord is swollen, painful, and constricted in the inguinal canal. The pain is sometimes intense, and accompanied by nausea and vomiting. Sometimes funiculitis is complicated by local peritonitis, or by abscess or hydrocele of the cord.

Spermato-cystitis or Vesiculitis.—This complication may occur in posterior urethritis, and may be associated with prostatitis or epididymitis. In acute spermato-cystitis the vesiculæ can be felt enlarged by rectal examination, but in chronic cases they are not so obvious.

Symptoms.—The most important sign of spermato-cystitis is the occurrence of blood-stained ejaculations (hæmospermia). These ejaculations are frequent and painful, and of a *café-au-lait* appearance, owing to the mixture of blood with the semen.

Spermato-cystitis may end in resolution or in suppuration, and may occur independently of epididymitis. If suppuration

occurs, the abscess may open into the urethra, or into the peritoneum, causing peritonitis. Chronic spermato-cystitis is one cause of *gleet*.

Treatment.—Acute cases require the same treatment as acute prostatitis. If suppuration occurs, the pus should be evacuated by a perineal incision, guided by a finger in the rectum, or by a rectal incision. In chronic cases Fuller recommends the plan of regularly emptying or 'stripping' the vesiculæ by digital manipulation. The bladder being full, and the patient in a stooping position, the forefinger is introduced into the rectum, and counter-pressure made above the pubes. The contents of the distended vesicles are thus pressed out into the urethra, and washed out when the patient evacuates the bladder. It would appear, however, that this procedure is of questionable value, and likely to light up further mischief by discharging latent foci of gonococci into the urethra.

Epididymitis.—This is another complication of posterior urethritis, and is caused by direct extension of the gonorrhœal inflammation along the vas deferens. It sometimes occurs without any sign of deferentitis. Violent exercise, excess of alcohol, irritating injections, etc., act as exciting causes. It may occur, however, in persons who have been properly treated, and it is possible that anomalies of the testicle favour the extension of gonorrhœa to the epididymis.

Diminution of the discharge at the onset of epididymitis gave rise to the theory that the affection was due to metastasis. This theory must now be abandoned, as it is known that the gonococci propagate directly from the urethra to the epididymis along the vas deferens, although the latter may be only slightly affected during the process. According to Cuneo, propagation takes place through the lymphatics communicating from the urethra to the epididymis in the submucosa of the vas deferens. Gonococci have been found in the epididymis by means of puncture, and also in pus from abscesses. In some cases deferentitis and funiculitis become more evident after the development of epididymitis.

Morbid Anatomy.—The walls of the vas deferens are

thickened, the epithelial cells lose their cilia and become round and granular, and the walls of the canal are infiltrated with leucocytes. Similar changes occur in the seminal tubules of the epididymis. According to Audry and Dalous, epididymitis is characterized by erosive and proliferating inflammation of the epithelium, with secondary lymphangitis around the tubules. On section, yellow foci are found, consisting of dilated tubules filled with epithelial cells, leucocytes, and spermatozoa. Later on the interstitial infiltration undergoes fibrous transformation, and the epithelial cells become changed from the ciliated cylindrical type to the cubical.

The testicle itself is rarely affected in gonorrhœal epididymitis, but its secretion is suspended, and it remains in an atonic condition after the epididymitis has subsided. The urethral discharge generally ceases during the course of epididymitis, to reappear when this has subsided.

Symptomatology. — Epididymitis generally occurs in the third or fourth week of gonorrhœa, but occasionally develops in the first week. On the other hand, it may occur much later as a complication of chronic urethritis.

It is generally preceded by pain along the spermatic cord, and a sensation of weight in the testicle. The testicle is enlarged, and painful on palpation. There is often some febrile disturbance. The intensity of the pain varies considerably, and is not always proportionate to the degree of swelling of the testicle. Sometimes the pain radiates to the loins or down the thigh ; it is always increased by walking, and the patient adopts a bent attitude, with the thighs everted.

On examination of the testicle the epididymis is found tender and enlarged, and the cord sometimes thickened. The enlargement of the epididymis begins at the lower part and extends rapidly upwards, forming a sort of helmet crest on the back of the testicle. The epididymis may be much increased in size, elongated, and irregular, and when there is funiculitis at the same time may cause torsion of the testicle with retraction, so that the displaced epididymis may be found at the side or even in front of the testicle.

The *tunica vaginalis* is generally affected with acute hydro-

cele, the amount of effusion varying in different cases. The inflammation generally extends beyond the tunica vaginalis, causing swelling and redness of the scrotum.

The febrile symptoms generally subside in four or five days, but relapses may occur in the course of epididymitis, with a rise of temperature on each occasion. Constipation is a common symptom, and nausea and vomiting not infrequently occur. When ejaculations take place the semen is mixed with pus, and often with blood, which indicates the coexistence of spermato-cystitis. Spermatozoa are sometimes absent even in unilateral epididymitis, a fact which is explained by the existence of partial deferentitis on the other side. The prostate is often swollen and painful, and spermato-cystitis is a frequent complication.

The course of epididymitis includes a period of increase of three to six weeks, a stationary period of about a week, and a period of decline. Resolution in favourable cases is complete between the fifteenth and thirtieth day, but induration of the gland may remain for months. Hydrocele may also persist and become chronic. Suppuration is exceptional, but cases have been recorded by Ricord and others in which suppuration occurred, with hernia testis. Double epididymitis is not uncommon, but the two sides are affected successively. Alternate attacks may affect the two organs. Double epididymitis usually results in *sterility*. In single epididymitis sterility is usually only temporary, and is due to double deferentitis.

The *prognosis* of epididymitis is usually favourable except as regards the function of the organ in bilateral cases. However, gonorrhœal epididymitis may act as a predisposing cause to tubercular orchitis.

Diagnosis.—This is easy except when epididymitis occurs as a complication of chronic latent urethritis, but in these cases the presence of filaments in the urine usually reveals the origin of the complaint.

Tuberculous epididymitis is more nodular, with points of softening and adherence to the skin, but certain acute forms of tuberculosis of the epididymis and cord may evolve, with

local and general symptoms analogous to those of gonorrhœal epididymitis.

Syphilitic epididymitis has less acute symptoms and is less painful. It is nearly always double; the cord is not affected, and the epididymis presents only a few disseminated nodules.

Retained testicle, when affected with epididymitis, may be mistaken either for inguinal bubo or for strangulated hernia.

Treatment.—This includes rest in bed; raising the testicles by means of a T-bandage; frequently renewed cold compresses or ice-bags. Sometimes hot applications act better than cold, and hot enemata often give relief when there is concomitant prostatitis or vesiculitis. If there is much effusion into the tunica vaginalis, this should be punctured. Some authorities have advised puncture of the epididymis. Opium and belladonna suppositories are useful if there is much pain. The bowels should be kept open by laxatives, and salol or salicylate of soda are the best drugs for internal administration. No irritating applications should be applied to the scrotum, and the mercurial ointment which is sometimes recommended is of doubtful value. Glycerine and belladonna is a useful application, and if there is much tension leeches may be applied. The patient should keep his room for a fortnight, and when he goes out after this the testicles should be suspended by bathing-drawers or a triangular bandage. The usual suspensory bandage sold in shops is generally useless, as it is made to fit testicles of normal size and not enlarged ones.

With regard to local treatment of the urethra during epididymitis, both Finger and Balzer are of opinion that it should be suspended till the acute stage of the epididymitis has subsided; Neisser and Jadassohn, on the other hand, advise the continuance of local urethral treatment during the whole course of epididymitis, unless the symptoms are very acute.

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CHAPTER XXV

GONORRHŒA IN THE FEMALE

According to Finger, the parts affected by gonorrhœa in women are, in order of frequency, the urethra, cervix uteri, Bartholin's ducts, and the vagina. The vaginal epithelium is more resistant to gonococcal invasion than the other parts, and is usually affected by extension from the vulva. From the cervix uteri the gonorrhœal infection may extend to the uterus, Fallopian tubes, ovaries, and peritoneum. According to Baermann, the cervical canal is the only part affected in 46 per cent. of female gonorrhœa.

Gonorrhœa in women often passes unrecognised, owing to the mildness or absence of symptoms. There may be smarting on micturition and painful swelling of the labia, causing varying degrees of discomfort, but the acutely painful symptoms of gonorrhœa in the male are usually wanting. Neisser examined 527 prostitutes who showed no visible sign of the disease, and found gonococci present in 126. This, however, does not prove that all these women were infected with gonorrhœa, for, as Jullien has pointed out, gonorrhœal pus may remain in the vagina for several hours without infecting it. In this way one man may contract gonorrhœa from another, the woman acting as an intermediary agent. This may lead to the blame being thrown on the wrong person.

Vulvitis.—Gonorrhœal vulvitis is generally accompanied by urethritis or vaginitis. The symptoms consist in heat and itching of the parts, followed by redness and swelling and discomfort in walking. The purulent discharge is liable to cause intertrigo and erosions of the labia. Lymphangitis and suppurating bubo are uncommon. Some cases become chronic,

owing to extension of the inflammation to Bartholin's ducts and the follicles of the mucous membrane of the vulva.

Gonorrhœal vulvitis may be mistaken for simple vulvitis due to want of cleanliness, which is analogous to circinate balanitis in men (p. 173), or for herpes, which sometimes suppurates freely after rupture of the vesicles. Diagnosis is established by the presence of the gonococcus in the pus.

Bartholinitis.—Gonorrhœal inflammation may be limited to the duct of Bartholin's glands, or may affect the gland itself and the periglandular tissue. The affection may be unilateral or bilateral, and the gonococcus is often associated with other micro-organisms. The cylindrical epithelium of the gland is said to undergo the same modification into flat cells which occurs in chronic urethritis.

Acute Bartholinitis is manifested by acute inflammatory swelling of the lower part of the labium majus. This is soon followed by acute œdematous swelling of the whole labium and of the labium minus. Pus can be expressed from the canal of the gland on the inner surface of the labium. Fistulous tracts may be formed if the pus is not evacuated early.

Chronic Bartholinitis is very common, and often passes unnoticed unless an acute exacerbation takes place. The inflammation may be limited to the duct, which becomes dilated and cystic if its orifice is obliterated. The orifice of the duct is sometimes ulcerated, and surrounded by projecting granulations. Pressure on the duct causes purulent discharge, containing gonococci, which gives rise to fresh infection of the genital organs. Chronic Bartholinitis is one of the common forms of latent gonorrhœa, by which women who are apparently healthy cause gonorrhœal infection in men. After spontaneous or surgical opening of the abscess, fistulous tracts may remain leading to the vulva, vagina, perineum, or rectum.

Vaginitis.—Although the vaginal epithelium is more resistant to the gonococcus than the epithelium of other parts of the genito-urinary system, it may be affected primarily in girls and young women, and also in pregnant women of maturer age. The vaginal infection is more commonly

secondary to gonorrhœal vulvitis, Bartholinitis, urethritis, or endocervicitis, and the gonococcus is often associated with staphylococci, streptococci, and the coli bacillus.

The vaginal mucous membrane is red and granular, owing to swelling of the papillæ. The discharge is yellow or greenish-yellow, and contains mucus, pus, and epithelial cells. The gonococcus is sometimes difficult to find in the multitude of other organisms which develop in the pus. The discharge is usually the first sign of the disease, but this may be preceded by burning sensation and pelvic pain.

In some cases the whole of the vagina and cervix are affected, and the inflammation may spread to the submucous tissue, and even form an abscess along the vagina. In other cases the vaginitis is diphtheroid, and the vagina is covered in places with membranous deposits adherent to the rough and granular mucous membrane.

The duration of acute vaginitis is variable, but the acute symptoms usually subside after a fortnight, and the inflammation becomes subacute. Relapses are, however, liable to occur, especially during menstruation, which explains the popular idea that a man may contract urethritis by connection during menstruation.

Chronic vaginitis may follow the acute form, or may be secondary to endocervicitis. The mucous membrane is red or gray, with red papillæ and erosions of the cervix. In long-standing cases of chronic vaginitis the mucous membrane of the vagina becomes xerotic and of leathery consistence. Chronic vaginitis is always accompanied by endocervicitis.

Diagnosis is often difficult to establish from leucorrhœa in the absence of gonococci, and it must be borne in mind that a large proportion of cases of leucorrhœa are the remnants of former gonorrhœa, in the same way that gleet in men, although non-gonococcal, is the remnant of former gonorrhœal urethritis.

Urethritis.—Gonorrhœal urethritis in women may be acute or chronic, but seldom gives rise to such acute symptoms as in the male. It is usually associated with vulvo-vaginitis. In acute urethritis the meatus is red and swollen, and a purulent discharge containing gonococci can be expressed

from the urethra. In chronic urethritis the discharge is muco-purulent, and the urine contains filaments.

The urethritis may be total, but is more commonly confined to the external part of the urethra. It becomes localized in the lacunæ and follicles of the mucous membrane, and in some cases may cause fibrous thickenings. Stricture is rare, but has been observed. Sometimes the process affects the follicles of Astruc, which are situated on each side of the meatus; these follicles become swollen and indurated, and may give rise to perifollicular abscesses, followed by fistula opening into the urethra or vagina.

In chronic cases the urethra becomes dilated, and the lower wall forms a pouch which becomes constantly filled with pus (vaginal urethrocele). Occasionally the urethral mucous membrane becomes covered with small vegetations which may almost fill the canal.

Endocervicitis—Endometritis—Metritis.—Gonorrhœal endocervicitis may be due to primary infection of the uterus with gonorrhœal discharge from the male, or may be secondary to vaginitis. The uterus is the most common seat of chronic gonorrhœa in women, and this explains the frequent cases in which men contract gonorrhœa from a woman who has no sign of gonorrhœal affection of the external genitals.

The gonococcus develops in the cervical canal, and invades the uterus secondarily. The gonorrhœal process may thus be limited to *endocervicitis*, or may extend to the cavity of the uterus, giving rise to *acute endometritis*, or *acute metritis*, in which the muscular tissue of the uterus is invaded by way of the lymphatics.

According to Menge, the cervical mucus acts as a barrier to all microbes except the gonococci.

Symptoms.—The affection of the uterus is usually insidious in evolution, and causes little or no symptoms, except discharge of muco-purulent matter from the vagina. In acute cases, however, there is pain in the hypogastric region, radiating to the loins and sacrum. This is increased on movement and exacerbated by menstruation, and in severe cases the patient may be confined to bed. The uterus is found to be swollen

on bimanual examination, and this proceeding is usually painful.

Acute or chronic endometritis differs according to whether the subject has been pregnant or not. In nulliparæ acute endocervicitis is accompanied by swelling of the mucous membrane, which projects from the external os and constricts it. There are nearly always red erosions of the vaginal portion of the cervix.

In *chronic metritis* the cervix is increased in size, and is seen by the speculum to be red and swollen, with erosions about the external os. The latter is filled with an adherent plug of mucus, which is difficult to detach. After a time the cervix may attain a considerable degree of hypertrophy, and may become much elongated. In women who have had children the os is more patulous and the discharge escapes more easily.

The inflammatory process may assume different forms—simple muco-purulent catarrh, fungating or hæmorrhagic endometritis, or fibrous endometritis, resulting in cicatricial stenosis of the os.

In many cases chronic gonorrhœal metritis remains latent for a long time, and is only manifested by a chronic leucorrhœal discharge. In some cases there is affection of the general health, manifested by anæmia, neuralgia, neurasthenia, and digestive disorders, and sometimes there is pain after menstruation.

The metritis is liable to recrudescence at the menstrual periods, and constitutes a perpetual danger for the woman by hæmorrhages, and by its complications, which include abscess in the broad ligament, local or general peritonitis, salpingitis, and ovaritis.

Puerperal Endometritis. — Gonococcal invasion of the body of the uterus is favoured by the puerperal state. Gonorrhœal endometritis is a common cause of sterility, but pregnancy may occur in spite of it. It is also a cause of abortion and of peri-uterine inflammation. The occurrence of pregnancy causes recrudescence of latent gonorrhœa, which takes on fresh activity and more extensive development. The uterus remains enlarged, with a dilated cervix and fungating

cavity, and is liable to prolonged metrorrhagia. The lochial discharge contains gonococci, and there is often some fever.

Puerperal gonorrhœal endometritis often explains cases of 'one-child sterility.'

The true cause of these accidents is often not recognised, for they sometimes do not appear till several weeks after confinement. The wall of the uterus is invaded by gonococci, and parametritis, salpingitis, oophoritis, perimetritis, or general septicæmia may result. The gonococcus has been known to cause suppuration in the points of suture in cases of Cæsarian section (Hecking). The gonococcus is often the cause of the so-called *puerperal rheumatism*. During the evolution of these complications the gonococcus may be associated with other pyogenic cocci, and, according to Fruhinsolz, the gonococcus disappears before these secondary organisms, the invasion of which it has favoured, and a condition of *paragonorrhœic* infection remains. In some cases old gonorrhœal lesions of the ovaries, tubes, or peritoneum revive during labour.

Diagnosis.—The diagnosis of gonorrhœal endocervicitis and endometritis is often difficult in cases where there is no evidence of gonorrhœal affection of the external genital organs. Search must be made for the gonococcus in the uterine discharge, but in cases of chronic endometritis this organism is often difficult to discover among the numerous other microbes which are usually present (staphylococci, streptococci, and coli bacilli, etc.). According to Jersild, in non-gonococcal endocervicitis the discharge is mucoid and transparent, and does not contain gonococci, whereas in chronic gonorrhœal endocervicitis the discharge is turbid, and contains many epithelial cells, a few leucocytes, and gonococci. Jersild found gonococci in 90 per cent. of cases of endometritis occurring in prostitutes. According to Schultze, diagnosis of gonorrhœal endometritis may be made by examining the secretion collected by a tampon placed for twenty-four hours against the cervix. The presence of streaks of pure pus, not mixed with muco-pus from the cervix, indicates endometritis.

Apart from a purulent discharge containing gonococci, the occurrence of ophthalmia neonatorum within three days after

birth may be accepted as evidence of gonorrhœa in the mother.

Salpingitis, Ovaritis, and Perimetritis.—Gonorrhœa is the most common cause of salpingitis and ovaritis, by extension of the gonococcal invasion from the uterus to the Fallopian tubes and ovaries. From the tubes the inflammatory process extends to the pelvic peritoneum, giving rise to pelvic adhesions, which may involve the ovary and cause occlusion of the tubes. In this way gonorrhœa in women leads to a condition of chronic pelvic inflammation, which accounts for many cases of *chronic invalidism*, especially in young married women who have been infected by latent gonorrhœa in the husband. This pelvic inflammation, by occlusion of the Fallopian tubes, may cause sterility or extra-uterine pregnancy.

Gonorrhœa is thus the most common cause of *sterility*—in women by chronic endometritis and cicatricial stenosis of the internal os, by occlusion of the Fallopian tubes from pelvic inflammation, or by extension of the inflammation to both ovaries; in men by double epididymitis, causing occlusion of the seminal tubules or vasa deferentia on both sides.

Pyosalpinx.—Acute gonorrhœal pyosalpinx may occur, and is more common on the left side. This may be due to secondary infection from the rectum.

Peritonitis.—General peritonitis may be caused by extension of the gonococcal infection from the Fallopian tubes and uterus. Cushing described two cases in women in which laparotomy was performed; gonococci were found in the peritoneal fluid. Hunner and Harris recorded several cases of pyosalpinx and peritonitis of gonorrhœal origin in which gonococci were found in the tubes and in the peritoneal effusion. Cases of gonorrhœal peritonitis secondary to vulvo-vaginitis in young girls have also been reported.

Diagnosis.—The symptoms of gonococcal peritonitis are the same as in other forms of peritonitis—viz., abdominal distension, tenderness and rigidity, vomiting, high temperature, and quick pulse. The affection, however, is characterized by its sudden onset and usually rapid abatement of symptoms.

The usual mistake in diagnosis is that of *appendicitis*, especially when the peritonitis is limited to the pelvis. The presence of leucorrhœa or vaginal discharge, irritability of the bladder, and the onset of symptoms during or directly after menstruation, are in favour of gonorrhœal peritonitis.

Gonorrhœa in Children.

Gonorrhœa in children generally occurs in the female in the form of *vulvo-vaginitis*. Kimball found 70 cases of vulvo-vaginitis in 600 admissions to the Babies' Hospital in New York. He also reports eight cases of gonorrhœal pyæmia occurring in infants under three months old—seven males and one female. In six of these cases there was polyarthritis, affecting chiefly the knees, ankles, and wrists, and gonococci were found in the pus from the joints. No urethritis, vaginitis, or conjunctivitis were found to account for the infection, but in three cases there was stomatitis in which a diplococcus was found resembling the gonococcus in its appearance and staining reaction. Kimball therefore considers that the point of origin of the infection was gonorrhœal stomatitis. This was supported by the fact that in one case there were tracheal abscesses containing gonococci, pointing to entry by the respiratory tract.

Northrup reports two cases of peritonitis consecutive to vulvo-vaginitis in girls aged nine and eleven years. Gonococci were found in the vaginal discharge, and the source of infection was found to be a woman affected with gonorrhœa with whom the children slept. One of these cases was operated on for appendicitis, but no cultures were taken from the peritoneum. Comby recorded eight cases of vulvo-vaginitis with varying degrees of peritonitis, all of which recovered without operations. Variot also reports two cases of gonococcal vulvitis and peritonitis in two sisters aged ten and twelve years. Both recovered without operation.

These cases of peritonitis secondary to vulvo-vaginitis are usually benign, but fatal cases have been reported by Huber and Baginsky. They are of rapid evolution, and it is possible that extension occurs by the lymphatics, and not directly from the uterus and tubes.

Treatment of Gonorrhœa in Women.

In acute cases the patient should be kept in bed, the bowels regulated by saline cathartics, and an unstimulating diet administered. Frequent hot baths are useful, and the vulva and vagina should be irrigated with permanganate of potash (1 in 5,000) at least twice daily. Salol may be given internally, but balsams should not be administered during the acute stage, and are only of use in cases of urethritis.

After the acute stage has passed the affected parts should be thoroughly treated with *nitrate of silver* (1 per cent.) or *protargol* (2 to 5 per cent.). This can only be thoroughly performed with the patient in the lithotomy position and through a Sims' speculum. The vagina and cervix should be wiped dry, and the solution applied with a swab. The urethra, cervical canal, and Bartholin's ducts should be treated by injection of the same lotion by means of a small syringe. This should be done every other day.

In the intervals between these applications wool tampons impregnated with a glycerine solution of *ichthyol* (2 to 5 per cent.) may be placed high up in the vagina against the cervix.

An improvement on the wool tampon is the *glycerine-gelatin pessary*, which is placed in the posterior vaginal cul-de-sac and left there during the night. These pessaries gradually melt, and lubricate the vaginal wall. The best results, in the author's practice, were obtained with pessaries made with ichthyol (2 to 5 per cent.) or iodine (1 per cent.).

In suppurative *Bartholinitis* the abscess must be incised and the cavity irrigated with permanganate lotion, and afterwards swabbed with chloride of zinc (1 in 20). In chronic cases it may be necessary to dissect out the gland.

In *endocervicitis* and *endometritis* all instrumental treatment must be avoided during the acute stage, as this may lead to extension of the inflammation to the tubes and ovaries. After the acute symptoms have subsided, the cervical canal should be treated with sulphate of copper solution, applied by means of a Playfair's probe lightly covered with wool. Iodized phenol is also useful in obstinate cases.

In cases of chronic endometritis, intra-uterine irrigation with permanganate of potash, followed by the instillation of a few drops of nitrate of silver (2 per cent.) or protargol (5 per cent.), should be tried. If this fails, the cervix should be dilated with Hegar's dilators, the uterine cavity scraped with a flushing curette, and iodized phenol applied to the whole surface. The best form of curette is one similar to Barker's flushing curette; most of the uterine curettes in the market have the scraping end too large and the flushing tube too narrow. During the scraping a solution of perchloride of mercury (1 in 5,000) is passed through the curette by an irrigator apparatus.

Perimetritis and *salpingitis* must be treated by absolute rest, hot vaginal douches, enemata, and morphia suppositories if required.

J. W. Taylor has pointed out that many cases of salpingitis in which there is no history of syphilis, but only one of gonorrhœal infection, improve and get permanently well after a prolonged course of *mercury* and *iodides*, provided the disease stops short of acute pyosalpinx.

It therefore appears rational to administer a course of *mercury* and *iodides* in all cases of chronic gonorrhœa and its complications, both in the male and the female, especially as there is always a possibility of concomitant syphilitic infection. Mercurial treatment for gonorrhœa was suggested recently by Morel Lavallée in cases of gonorrhœal rheumatism.

Acute pyosalpinx should be treated by free incision of the posterior vaginal fornix, by thorough exploration and emptying of all pus cavities, and by iodoform drainage. This is preferable to the older operation of removal of the appendages, which is more dangerous. Occlusion of the tubes and peritoneal adhesions due to salpingitis will remain after the gonorrhœal process has subsided, and sterility may result, although the gonorrhœa may be cured. Some cases of pelvic gonorrhœa remain intractable, especially when complicated with uterine fibroids, etc. In these cases removal of the affected organs may be required, and vaginal hysterectomy, with or without removal of the appendages, is the most rational operation (Taylor).

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CHAPTER XXVI

GENERAL INFECTION IN GONORRHŒA

GONORRHŒA, which is at first a local affection, may cause general infection of the system by diffusion of the gonococcus or its toxins (gonorrhœal septicæmia). How far this general infection occurs in ordinary cases is at present unknown, but it is possible that the usual signs of general infection are only an exaggeration of a condition which, as a rule, remains latent. The gonococcus has been found in the blood by many observers, as well as in the metastatic foci. It is also probable that some of the effects of generalized infection are due to the action of the *gonotoxin*. The gonococcal infection is sometimes complicated by the association of the gonococcus with pyogenic organisms. Balzer and Lacour have found the *Staphylococcus albus* with the gonococcus both in the blood and in the urethra; and mixed infections with gonococci, streptococci, pneumococci, etc., originating in gonorrhœa, have been reported. In this way a condition of *gonorrhœal pyæmia* is produced.

The principal manifestations of general gonorrhœal infection consist in *arthritis* (gonorrhœal rheumatism) and *endocarditis*. In addition to these, neuritis and affections of the central nervous system, ophthalmia, pleurisy, sometimes occur, and certain cutaneous affections have been described. General peritonitis may occur, but is usually secondary to gonorrhœal inflammation of the female genital organs.

Gonorrhœal Arthritis.—Whether the rheumatic diathesis predisposes to gonorrhœal arthritis is a matter of opinion, and of little consequence; what is more important is the fact that many cases of so-called rheumatism are of gonorrhœal origin,

which is either overlooked or dissimulated. Attacks of 'rheumatism' occurring in young men are always suspicious of gonorrhœa; and the same applies to young married women, who are frequently infected by their husbands with a latent gonorrhœa, which they may believe to have been cured.

The gonococcus is often found in the joints in cases of gonorrhœal arthritis, and it is probable that this microbe is capable of producing inflammation of the synovial membranes without the assistance of other pyogenic organisms.

Gonorrhœal arthritis is more common in men than in women, but may occur in the latter as a complication of gonorrhœal endometritis. It has also been observed in children after gonorrhœal urethritis, vulvo-vaginitis, or even ophthalmia. The affection may thus be due to gonorrhœal infection arising from any source, but is especially a complication of *posterior urethritis in the male*. It most commonly appears in the second or third week of acute urethritis, but may occur in chronic cases, or during recrudescence of a latent gonorrhœa.

The large joints are most often affected, especially the knee, the smaller joints being usually affected after the larger ones, and seldom primarily. The arthritis is usually polyarticular at first, but may afterwards become localized to a single joint. The following table, taken from Finger, shows the relative frequency of the joints affected in 376 cases:

Knee	136
Ankle	59
Wrist	43
Digits	35
Elbow	25
Shoulder	24
Hip	18
Temporo-maxillary	14
Metatarsal	7
Sacro-iliac	4
Sterno-clavicular	4
Chondro-costal	2
Intervertebral	2
Tibio-fibular	1
Crico-arytenoid	2
	376

Gonorrhœal arthropathies may be divided into four types: arthralgia, hydrarthrosis, arthritis, and polyarthritis deformans.

1. ARTHRALGIA.—This is manifested by pain in the joint only, without effusion or inflammatory phenomena. It is often accompanied by myositis or tenosynovitis.

2. HYDRARTHROSIS.—In this form there is effusion into the joint, generally one or both knees, without local inflammatory symptoms. The effusion takes place rapidly, and is liable to become chronic, leaving a weak joint.

3. ARTHRITIS.—This is the most common form, and constitutes the so-called gonorrhœal rheumatism. The arthritis is generally of the *sero-fibrinous* type, but occasionally suppuration occurs, with the usual signs of suppurative arthritis. It usually begins in several joints at first, most commonly the knees and ankles, but later on may be localized to one joint only. In other words, gonorrhœal arthritis is at first polyarticular, with a tendency to become monarticular subsequently.

The onset may be acute or insidious, with effusion into the joint, pain and limitation of movement, and sometimes inflammation of the periarticular tissues. There is often a rise of temperature, but febrile symptoms are less marked than in ordinary rheumatism. The sour sweat and concentrated urine of acute rheumatism are absent. Resolution generally occurs in the course of a few weeks, but there is a tendency to fibrous ankylosis unless measures are taken to prevent it. There may also be some muscular atrophy. The knee-joint is affected far more frequently than any other joint; but affection of the sterno-clavicular and temporo-maxillary joint, although uncommon, is suspicious of gonorrhœal arthritis. The affection generally occurs during the course of posterior urethritis, but may occur in the first week of gonorrhœa. It is often accompanied by myositis and tenosynovitis. A characteristic symptom of gonorrhœal rheumatism is *pain in the heel*, due to affection of the osteofibrous attachments to the calcaneum and implication of the internal plantar nerve. Suppuration is rare in gonorrhœal arthritis, and is due to secondary infection with pyogenic cocci.

Diagnosis.—The following table shows the chief points of difference between gonorrhœal arthritis and subacute rheumatism:

Gonorrhœal Arthritis.	Subacute Rheumatism.
1. Seldom affects more than two or three joints. Becomes often localized to one joint. Less migratory from one joint to another. Usually affects knees.	Affects several joints, and usually migrates from one to another. Affects wrists and ankles more than knees.
2. Pain slight in absence of movement, unless suppuration.	Pain considerable in absence of movement.
3. Fever slight or absent.	Well-marked fever, as a rule; profuse and sour sweat.
4. Urine often contains filaments from posterior urethritis; otherwise normal.	Urine concentrated and of febrile type.
5. Usually occurs during posterior urethritis or after recent gonorrhœa.	

Syphilitic Arthritis.—Synovial effusion occurring in secondary syphilis may be mistaken for gonorrhœal arthritis; but it differs in being less acute, in affecting fewer joints, in the absence of pain, and in the presence of other signs of secondary syphilis. The later forms of syphilitic arthritis, in which there are perisynovial or osseous gummata, cannot be mistaken for gonorrhœal arthritis.

It must be remembered, however, that a patient often contracts syphilis and gonorrhœa at the same time. Hence gonorrhœal rheumatism may occur during the course of secondary syphilis, or syphilitic hydrarthrosis may coincide with posterior urethritis. It is also possible that the joints might be affected by the combined action of the two poisons. Such cases should be treated with a combination of mercury and iodides, which is useful also in gonorrhœal arthritis.

In all cases of rheumatism occurring in young men or in those who have had gonorrhœa the urine should always be examined for filaments or 'clap-threads,' the discovery of which will give a clue to the origin of the complaint. Gonorrhœal

arthritis in a patient who has once suffered from it is liable to recur at each fresh attack of urethritis, or at each recrudescence of a latent gonorrhœa. In women gonorrhœal arthritis is less common, but, according to Lorimer, many cases occur after *leucorrhœa*, and are mistaken for rheumatoid arthritis.

Polyarthritis Deformans.—This is a more rare form of gonorrhœal arthritis, which was first described by Fournier. It affects the interphalangeal, metacarpo-phalangeal, and metatarso-phalangeal joints of the fingers and toes in the form of periarticular fibrous thickening and osteophytic outgrowths from the bone. It may affect the great toe and simulate gout. It differs from rheumatoid arthritis in only affecting one, two, or three digits. Fournier describes cases coinciding with other signs of gonorrhœal rheumatism, and occurring with successive attacks of gonorrhœa; 'the successive repetition of the same phenomena under the same conditions shows their pathogenic connection.'

Gonorrhœal Arthritis in Children.—Gonorrhœal arthritis in children is generally polyarticular, and affects the small joints of the hands and feet more often than the wrist, knee, or ankle. Halle has reported several cases of gonorrhœal arthritis consecutive to vulvo-vaginitis. In one case the sterno-clavicular joint was affected in a girl aged seven. In another case—a girl aged five—there was arthritis of the hip-joint, supposed to be tuberculous; there was, however, no pain in the knee, no lameness, and vulvo-vaginitis was discovered.

Clement Lucas reported 23 cases of joint disease in infants following purulent ophthalmia. Of the 23 cases, 18 had ophthalmia neonatorum contracted during parturition, and 5 were due to secondary inoculation in older children. The joint disease generally appeared in the second or third week of the ophthalmia, and chiefly affected the knees and wrists. Gonococci were found in the discharge from the eyes and in the joints. The form of arthritis was sometimes acute, sometimes only a subacute synovitis. It differed from syphilitic joint affection in appearing earlier and pursuing a more rapid course.

Tenosynovitis.—Effusion into the tendon sheaths usually

coexists with gonorrhœal arthritis, but may occur independently. The effusion, in which gonocooci have been found, is usually serous, but occasionally purulent. The tendon sheaths most often affected are those of the peronei, tibialis anticus and posticus, extensors of the fingers and toes, flexor pollicis, semi-membranosus and semi-tendinosus.

Bursitis.—The bursæ are less commonly affected in gonorrhœal infection than the tendon sheaths; the retrocalcaneal and subcalcaneal are the ones most often involved.

Treatment.—Opinions differ as to whether local treatment of the urethra should be continued during an attack of gonorrhœal arthritis. Some advocate energetic irrigation of the urethra, while others advise suspension of urethral treatment. Although the posterior urethra is the origin of the infectious process, it would appear to be the wisest course to suspend irrigation or injections during the acute stage.

Internally, salol is useful in all cases of chronic urethritis, although it is doubtful if it has much effect on the joint affection. The best internal treatment seems to be that by the administration of *mercury* combined with *iodides*, advocated by Morel-Lavallée. This is especially useful in chronic cases.

Local treatment consists of immobilization of the affected joints during the acute stage, with the application of ice-bags; but the joint should not be fixed for too long a period, owing to the tendency to the formation of fibrous adhesions. After the acute symptoms have subsided, a course of massage combined with hydrotherapy is indicated. Balzer recommends the application of an ointment of guaiacol (5 per cent.) to the affected joint, and others advocate mercurial ointments. Some have tried intravenous injections of collargol, and others intravenous injections of perchloride of mercury; but these procedures seem to be unnecessarily heroic and of doubtful benefit. The Tallerman hot-air bath has given good results, according to some observers. In the rare cases which suppurate the joint must be opened, drained, and irrigated in the usual way.

Endocarditis.—The knowledge of the cardiac complications of gonorrhœa is of comparatively recent date, the first

case of gonorrhœal endocarditis being reported by Brandes in 1854. It was formerly stated that gonorrhœal rheumatism differed from ordinary rheumatism in not affecting the heart, but this idea is now exploded.

Endocarditis, pericarditis, and myocarditis may occur during the course of gonorrhœa, with or without coincident arthritis. The commonest affection is endocarditis, pericarditis is comparatively rare, and myocarditis is secondary to one of the other two. Old-standing valvular lesions may also be aggravated by general gonorrhœal infection.

Gonorrhœal endocarditis usually occurs during the first few weeks of acute gonorrhœa—sometimes during the first week. It may be insidious in onset, and give rise to no symptoms, or may begin with fever, palpitation, dyspnœa, and precordial pain. It may subside and leave no trace, or may result in valvular lesions. The physical signs are the same as those of ordinary rheumatism, and generally indicate mitral regurgitation, sometimes aortic regurgitation, less often mitral or aortic stenosis. The right heart is sometimes affected secondarily to the left.

Ulcerative Endocarditis. — In some cases gonorrhœal endocarditis assumes the type of malignant or ulcerative endocarditis, with high fever and rigors, ending in a typhoid state, with embolic infarcts and pyæmia. Such cases are due to mixed infection with gonococci and pyogenic organisms, and are invariably fatal. Ulcerative endocarditis generally occurs during chronic urethritis, and often coexists with arthritis or epididymitis. It usually affects the aortic valves.

Bacteriology.—The gonococcus has been found in valvular lesions and in the myocardium by Finger, Ghon, Schlagenhaufer, Krause, and others; and in cases of malignant endocarditis streptococci, staphylococci, and pneumococci have also been found. In the malignant cases of mixed infection in which there is high fever the gonococcus loses its vitality at a temperature of 39° or 40° C., while the pyogenic cocci survive. Beurmann reported a case of purulent pericarditis in which gonococci were found in the pus.

Diagnosis. — Symptoms of palpitation, dyspnœa, irregular

action of the heart, and precordial pain, occurring during an attack of gonorrhœa, are suggestive of gonorrhœal endocarditis or pericarditis. Moreover, when the same symptoms occur in a young or otherwise healthy subject, examination of the genital organs may reveal the origin of the complaint. Prognosis is good in most cases of endocarditis and pericarditis; but chronic valvular lesions may remain, and cerebral embolism has been recorded.

Gonorrhœal affections of the heart are probably more common than is generally supposed, because it is not the custom to examine the heart as a routine procedure in gonorrhœa, as it is in rheumatism. In fact, the part played by both syphilis and gonorrhœa in the causation of heart disease is largely ignored, and nearly all heart affections are attributed to rheumatism and gout.

Phlebitis.—Gonorrhœal phlebitis may be due to infection of the veins directly from foci of gonorrhœal inflammation, or indirectly as a part of general gonococcal infection. Heller has reported a case of phlebitis of the veins of the leg consecutive to gonorrhœal prostatitis and phlebitis of the pampiniform plexus. Brouardel has recorded a case of fatal pulmonary embolism due to gonorrhœal phlebitis.

Neuralgia. Sciatica.—Neuralgias and neuritis often accompany gonorrhœal rheumatism, or occur independently of it. Fournier long ago described *gonorrhœal sciatica*, and proved its connection with gonorrhœa by the following observations: (1) The sciatica often coexisted with gonorrhœal rheumatism or alternated with it; (2) it sometimes occurred during gonorrhœa independently of other signs of gonorrhœal rheumatism; (3) it was influenced by antigonorrhœal treatment.

Fournier quotes an example from Everard Home's work on urethral stricture (1803) concerning a patient who suffered from sciatica on four occasions, each attack occurring during the course of gonorrhœa. The last attack only yielded to treatment of the urethra for stricture. Gonorrhœa, therefore, appears to be well established as a cause of sciatica.

Gonorrhœal sciatica is characterized by its comparatively sudden onset, and by disappearing, as a rule, in the course of a

few days or weeks. Sciatica due to other causes is of more progressive evolution and generally longer duration. Gonorrhœal sciatica usually develops during the period of decline of the urethritis, in the second or third month. It is much more common in males than females. The *treatment* consists in treating the urethritis, the sciatica usually disappearing when the discharge ceases.

Multiple Peripheral Neuritis may occur during the acute period of gonorrhœa, usually in association with gonorrhœal rheumatism. It may be connected with lesions of the spinal cord or occur independently.

Meningo-myelitis.—A considerable number of observations have been recorded, tending to show that gonorrhœal infection may attack the spinal cord and meninges, either by the action of the gonococcus or by secondary infections. Menetrier reported the case of a man of forty-six who died after paralysis affecting all four limbs during acute gonorrhœa. Degenerative changes were found in the cells of the anterior horns and in the peripheral nerves.

Charcot was of opinion that in some cases paralysis originated in irritation of the nerve endings in the joints, tendons, and ligaments, and that this irritation might cause functional or even organic changes in the cord. However, in some cases of paralysis there is no previous affection of the joints, and Raymond suggests that these cases may be due to lesions in the anterior horns or peripheral nerves directly caused by the gonotoxin or gonococcus, which give rise to amyotrophy and arthropathy of trophic origin. The experiments of Moltchanoff on animals have shown that the gonotoxin produces changes in the cells of the anterior horns, the nerves, cerebral cortex, and the meninges. These lesions were more marked when the toxin of the streptococcus was mixed with the gonotoxin.

The *symptoms* of meningo-myelitis consist in lightning pains in the limbs, spasmodic paraplegia with exaggerated reflexes, and later on trophic disorders, anæsthesia, bladder and rectum affections, painful flat foot, and muscular atrophy affecting the foot, leg, and thigh. The affection generally occurs in young

men in the course of acute gonorrhœa, and varies with the exacerbations of the urethritis. The symptoms are improved by treatment, but may recur with a fresh attack of gonorrhœa.

Treatment.—As the urethra is the point of origin of fresh supplies of gonotoxin, energetic antiseptic irrigation of the urethra is indicated. The paralysis may be treated by sulphur baths, massage, and electricity.

Encephalopathy.—Transient or permanent delirium and acute mania have been stated to occur in the course of gonorrhœal rheumatism, or independently of it; also cases of sudden hemiplegia have been recorded. In a case of Pitres', a man of fifty-nine was attacked with hemiplegia and arthropathy of the wrist and elbow coincidently during gonorrhœa; two months later attacks of Jacksonian epilepsy occurred, which were followed by death. At the autopsy cerebral softening was found in the left Sylvian region.

How far these cerebral phenomena were due to the action of the gonotoxin it is impossible to determine in the absence of bacteriological confirmation; it is quite possible that they were caused by concomitant cerebral syphilis.

Nephritis.—Transient albuminuria frequently occurs in acute gonorrhœa in the absence of cystitis, which seems to show that it is due to general infection by the gonococcus or its toxins. Sometimes symptoms of acute parenchymatous nephritis occur, with general anasarca, and in these cases it is difficult to say whether the nephritis is gonococcal in origin or simply a coincidence. In most of the cases which have been published the nephritis ended favourably. Ahmann recorded a case in which the urine contained blood, albumin, and casts, in a patient suffering from gonorrhœal arthritis; gonococci were found in the blood during a rigor, and cultivated on ascitic agar. An inoculation of the fifth generation of this culture in a youth who volunteered for the purpose gave rise to gonorrhœal urethritis.

Pleurisy.—Cases of pleurisy, with or without effusion, have been described as occurring in the course of gonorrhœa, and in some cases the gonococcus has been found in the exudation. The prognosis is usually benign, and suppuration is rare.

Ophthalmia.—Apart from purulent gonorrhœal ophthalmia caused by direct inoculation of the conjunctiva with gonorrhœal pus (p. 415), the eye is subject to metastatic complications, from general gonorrhœal infection. The most important of these are conjunctivitis and iritis; dacryo-adenitis, tenonitis, and optic neuritis (Panas) have also been reported.

Gonorrhœal Conjunctivitis.—This was first distinguished from purulent gonorrhœal ophthalmia by Abernethy, and afterwards described by Ricord and Fournier. It is manifested by vascular injection and chemosis, but differs from the usual forms of conjunctivitis in the mildness or absence of pain, photophobia, and lachrymation. In other words, it is characterized by the contrast of functional symptoms with objective signs. The onset is acute, and the affection often alternates from one eye to the other. Resolution generally takes place in two or three weeks. The affection usually occurs in association with gonorrhœal rheumatism, and is liable to recurrences. Bacteriological examination of the secretion for gonococci is negative.

An interesting case of conjunctivitis associated with arthritis, probably of gonorrhœal origin, was recently reported by Murrell. A man of twenty-five was suddenly attacked by double conjunctivitis, followed in a few hours by inflammation of the wrist and knees. The temperature was 101·8° F., and the patient was sweating profusely. The wrist-joint was not involved, but there was effusion into the tendon sheaths of the extensor muscles. The knee-joints were swollen, hot, and tender, with effusion later on. There was no history or sign of gonorrhœa, the urine contained no filaments, and there were no gonococci found in the conjunctival secretion or in fluid aspirated from the knee-joint. The symptoms did not yield to salicylate or to iodide. The patient had several subsequent attacks, both of arthritis and conjunctivitis, of gradually increasing severity. Murrell thinks the case was probably one of gonorrhœal arthritis arising from conjunctival infection with attenuated gonococcal virus. Owing to the short interval of time between the appearance of the conjunctivitis and the joint affections, it

would, however, appear more probable that it was a case of coincident gonorrhœal arthritis and conjunctivitis. Direct inoculation of the conjunctiva even with attenuated gonococci usually sets up violent purulent ophthalmia. Although a positive bacteriological result from examination of the fluid from the joints confirms the diagnosis of gonorrhœal rheumatism, a negative result does not exclude it. The negative result in the case of the conjunctival secretion, however, is in favour of metastatic gonorrhœal conjunctivitis rather than primary gonorrhœal ophthalmia.

Gonorrhœal Iritis.—This complication was first described by Laurence and Mackenzie; Rollet showed that it often occurred in connection with gonorrhœal arthritis, and Ricord pointed out that it sometimes occurred independently. As a rule, it takes the form of *serous iritis*, but is sometimes plastic, hæmorrhagic, or even purulent, causing hypopyon. The symptoms consist in photophobia, lachrymation, circumorbital pain, circumcorneal injection, discoloration of the iris, fixation and contraction of the pupil. As a rule, one eye only is affected at a time, but the two eyes may be attacked alternately.

Gonorrhœal differs from syphilitic iritis in the pain being more pronounced, and in there being less tendency to plastic adhesions. It is chronic in nature and liable to recurrences, with or without fresh attacks of urethritis. It is sometimes complicated with *choroiditis*, or *keratitis punctata*.

The *treatment* consists in dilatation of the pupil with atropine, and administration of drugs which are recommended for gonorrhœal rheumatism. As there is always a possibility of the iritis being due to concomitant syphilis, a trial should be given to antisyphilitic treatment.

Cutaneous Affections.—Certain cutaneous eruptions have been described as occurring in the course of gonorrhœa, and to these Landowzy has given the name of *gonorrheides*. The most common of these are *erythemas*, which occur during acute gonorrhœa in the form of macular, papular, vesicular, or scarlatiniform erythema, or as erythema nodosum and multiforme. According to some authors, they are caused by the

gonotoxin; according to others, they are a form of angio-neurotic erythema. Scholtz, however, found gonococci in the pus from a case which assumed the form of *erythema nodosum*. It would therefore appear that both syphilis and gonorrhœa take part in the etiology of erythema nodosum. Balzer has reported a case of bullous dermatitis with trophoneurotic onyxis which occurred in the course of polyarticular gonorrhœal rheumatism.

PURPURA is sometimes observed in severe cases of gonorrhœa, and appears to be due to the action of gonococci, or to mixed infection with staphylococci (Balzer).

HYPERKERATOSIS has been reported by several observers in the form of a symmetrical eruption of conical horny projections, affecting the limbs, trunk, and scalp. This dermatosis sometimes coincides with gonorrhœal rheumatism, and is often associated with amyotrophy, disorders of sensation, and loss of the nails. According to Jacquet, the hyperkeratosis is a trophic disorder caused by affection of the nervous system by the gonotoxin.

SUBCUTANEOUS ABSCESS.—The gonococcus occasionally gives rise to subcutaneous abscesses, in which this organism is found in the pus. Gonococcal abscesses have also been reported as occurring in the muscles and in the cervical glands.

Gonorrhœal Pyæmia and Septicæmia.—In some cases gonorrhœa may give rise to general pyæmia. Such cases are generally due to latent foci in the prostate gland or in other parts of the genital tract, and their true origin is often not recognised.

Ulmann has reported five cases of fatal gonorrhœal pyæmia, in four of which prostatic abscesses were found at the autopsy. In three of these cases the diagnosis had been enteric fever, malignant disease of the prostate, and purulent cystitis. Wynn has recently published an account of three cases of pyæmia, in one of which the gonococcus was found in the blood during life. In all these cases the urethra was the primary origin of the infection. Hence the necessity of examining the genital organs and urethra in cases of obscure

pyæmia. In most of the cases the infection is probably due to the combined action of the gonococcus and other pyogenic organisms, but the gonococcus alone is apparently capable of producing general septicæmia on its own account.

Thayer has recently reported ten cases of *gonorrhœal septicæmia* in the Johns Hopkins Hospital, in six of which the gonococcus was identified by cultures during life from the blood. In three of the cases there was mixed infection with other organisms. In one patient the symptoms resembled those of enteric fever—continued fever, coated tongue, palpable spleen, and erythematous spots, etc.—but cultures from the blood showed the presence of the gonococcus. Thayer's cases show that continued fever occurring in the course of gonorrhœa may be due to gonorrhœal septicæmia, and that the course of this may resemble enteric fever.

Vegetations.

Venereal vegetations (gonorrhœal warts, or *condylomata acuminata*) are papillomatous growths, varying in size from a pin's-head to large cauliflower masses. They usually accompany gonorrhœal discharges, but are aggravated by any chronic discharge from the genital organs. They are autoinoculable, and appear to be due to some specific agent, possibly the *Spirochæta refringens*, which has been found in venereal warts by Schaudinn and Hoffmann.

The venereal vegetation is formed chiefly by hypertrophy of the Malpighian layer of the epidermis; the papillæ become elongated, but otherwise the dermis is unaltered. In the male they occur on the glans penis and prepuce, and sometimes within the urethra; in the female they develop on the labia and other parts of the vulva and within the vagina. In women they sometimes form large cauliflower growths on the labia and adjacent parts. They are especially liable to increase in size during pregnancy, but diminish after labour. Venereal vegetations may be hard, warty, and pedunculated, or soft and sessile; in the latter case they somewhat resemble syphilitic condylomata (hypertrophic papulo-erosive syphilide).

The vegetation differs from the syphilitic condyloma in being deeply subdivided or digitated, and confined to the epidermis only, while the condyloma involves the dermis. Vegetations may, however, develop on the top of syphilitic condylomata.

Treatment.—The best treatment for venereal vegetations is removal by scissors and subsequent cauterization with nitrate of silver, carbolic acid, or the thermo-cautery. Large cauliflower masses require removal under an anæsthetic by means of scissors and thermo-cautery. Bleeding is sometimes profuse. In the case of pregnant women, if the growth is sufficiently large to obstruct labour, it may be partly removed under local anæsthesia with ethyl chloride, and the operation completed subsequently.

Small warts may be treated with equal parts of subacetate of copper and savin powder, or by touching them with pure carbolic acid or acid nitrate of mercury.

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CHAPTER XXVII

VACCINE AND SERUM TREATMENT OF GONORRHŒA

DURING the last few years vaccines made from dead gonococci and various kinds of serum have been used in the treatment of gonorrhœa, chiefly in cases of general gonococcal infection, or 'gonorrhœal rheumatism.' Better results have been obtained with the vaccine than with antigonococcal serum. Brück considers that passive immunization with gonococcus antiserum is useless, but that active immunization with gonococcal vaccines is beneficial, especially in the complications of gonorrhœa and in general gonococcal infection. However, remarkable results have followed the use of antistreptococcic serum in some cases, possibly depending on secondary infection.

Vaccine Treatment.—An autogenous vaccine prepared from the patient's own gonococci is better than a heterogeneous vaccine prepared from a mixture of other gonococci, but the latter is often the only one available.

The dose administered has varied from 1,000 million to 1 million cocci. Cole and Meakins and Irons used doses up to 1,000 million, but Eyre and Stewart consider that smaller doses of 1 to 10 million given at short intervals are better than larger doses at longer intervals. Brück considers a sharp reaction and rise of temperature necessary for active immunization, and uses from 10 to 40 million cocci as a dose, while Reiter recommends doses of 1 to 3 millions in most cases. Friedlander thinks the smaller doses suitable for mild cases, the larger doses for severe cases. He points out, however, that the age and activity of the gonococci have to be considered as well as the number.

Some observers regulate the treatment by estimation of the

opsonic index, while others rely only on clinical signs. Cole and Meakins consider control by the opsonic index uncertain and unnecessary; Friedlander and Reiter recommend it in general gonococcal infection, but not in cases of localized foci of gonococci. Large doses are followed by a more pronounced negative phase than small doses. The injection should never be repeated during the negative phase.

Schindler points out that the vaccine has no bactericidal action on the gonococci, for the latter multiply in cases of acute gonorrhœa treated by vaccines, and epididymitis may develop in spite of this treatment.

Vaccine treatment appears to give the best results in cases of gonorrhœal arthritis, although beneficial effects have been reported in cases of epididymitis and prostatitis, both acute and chronic. In acute gonorrhœal urethritis most observers agree that it is of little use, but Eyre and Stewart recommend it in acute urethritis, and in chronic urethritis when the gonococcus is the only affecting organism present. In acute urethritis they give doses of 1 or 2 millions, repeated at short intervals. Butler and Long reported good results in acute vulvo-vaginitis in children.

Hale White has reported two cases of much interest:

1. A woman with symptoms of severe septicæmia; the vaginal discharge contained streptococci, but no gonococci, but the original infection was presumed to be gonorrhœal. Recovery took place after combined treatment with streptococcus and gonococcus vaccines. This case is interesting in the employment of two vaccines, one for the original and another for the secondary infection.

2. A woman with arthritis of the knees, ankles, and fingers; one ankle suppurated, and gonococci were found in the pus. Recovery took place after treatment with an autogenous vaccine cultivated from the ankle-joint. This case is interesting in the occurrence of suppuration, which is unusual in gonorrhœal arthritis.

Stockman, on the other hand, after treating nine cases of uncomplicated gonorrhœal arthritis, mostly with autogenous vaccines, came to the conclusion that this treatment had no

curative influence. In two of his cases fresh joints became affected during the treatment.

Gonococcal Reaction. — The question has arisen whether a cutaneous reaction, similar to those of Von Pirquet and others for tuberculosis, can be obtained in gonococcal infection. Irons describes a general and local gonococcal reaction after injection of vaccines, the former manifested by rise of temperature with increased pain and swelling of the joints (in cases of gonorrhœal arthritis), the latter consisting in redness and swelling at the site of injection. He considers the general reaction of value in the diagnosis of doubtful cases of arthritis, and remarks that the reaction has many points in common with the tuberculin reaction. Brück states that in persons infected with gonorrhœa there appears to be a hypersensitiveness of the skin, which manifests itself in a cutaneous reaction after inoculation with gonococcal vaccines. The practical difficulty in the application of a gonococcal reaction lies in the fact that the reaction varies with the dose, with the patient, and also probably with different preparations of vaccine. It is therefore impossible at present to fix a dose that will produce a cutaneous reaction. Irons says that large doses (up to 500 million) are usually required, but according to Eyre and Stewart such doses are not always safe. Stockman failed to get a distinct reaction with 150 million cocci. Hence we must conclude that a cutaneous gonococcal reaction is at present of little value in diagnosis, although the general reaction may be useful in doubtful cases of arthritis.

More recently, Watabiki has tried gonotoxins instead of vaccines, to produce a cutaneous reaction. He found that cases of gonorrhœal arthritis reacted, but cases of urethritis did not. He concludes that the antibodies necessary for the reaction are produced in general gonococcal infection, but not in local; hence that the cutaneous reaction is only of use in cases of general infection.

Serum Treatment.—Curiously enough, the best results with serum treatment in gonorrhœa appear to have been obtained with *antistreptococcic serum*. Parkinson and Fenwick reported two cases of gonococcal septicæmia which were cured

by rectal injections of 10 c.c. of polyvalent antistreptococcic serum—(1) a woman, aged thirty-nine, with symptoms of pyæmia, and apparently moribund, recovered after three injections; (2) a girl, aged eighteen, with symptoms of acute rheumatism, recovered after fourteen daily injections. In both cases gonococci were found in the vaginal discharge. These were not regarded as cases of secondary infection, for gonococci were found in the pleural exudation in each case, and in the knee-joint in one case. Parkinson also obtained good results in cases of gonorrhœal arthritis with this serum. Further, Salter has reported a case of recurrent purulent gonorrhœal urethritis which was reduced to a slight mucoid discharge after three rectal injections of 10 c.c. of polyvalent antistreptococcic serum. Concerning the mode of action of this serum, Parkinson suggests that it inhibits the growth of the gonococcus or neutralizes its toxins; Salter thinks it acts by raising the power of resistance of the tissues. Another possible explanation is the coexistence of secondary streptococcic infection in these cases.

With regard to *antigonococcic serum*, Rogers and Torrey, a few years ago, tried a serum obtained by intraperitoneal inoculation of the sheep with gonococci cultivated on ascites-agar. The results were said to be good in gonorrhœal arthritis, epididymitis, and iritis, moderate in chronic urethritis, and *nil* in acute urethritis. This serum has, however, been abandoned by most authorities in favour of vaccine treatment.

Complement Fixation in Gonorrhœa.—Soon after the application of the complement fixation test to the serum diagnosis of syphilis by Wassermann, Neisser, and Brück, Müller and Oppenheim tried it in gonorrhœa, and found that the serum of a patient with gonorrhœal arthritis gave a positive reaction, indicating that the serum in gonococcal infection contains a specific antibody for the gonococcus. Controls were made with the serum of patients free from gonorrhœa, and gave negative reactions. These results were confirmed by Brück. More recently, Schwartz and McNeil have tried the test in 324 cases. Controls were made from cases with no signs or history of gonorrhœa, and from cases of other diseases. All tests were performed in duplicate with both antisheep and

antihuman hæmolytic systems. The technique used was that of Wassermann's test for syphilis. The antigen was prepared from about a dozen different strains of gonococci, not from a single strain, for it was found that different strains varied considerably in their power of fixing complement. The cases tested included acute and chronic urethritis, both gonorrhœal and non-specific, chronic prostatitis, epididymitis, and arthritis. In acute anterior gonorrhœal urethritis the reaction was negative, probably because the absorption of toxins was insufficient to produce antibodies. In most of the other cases the reaction was positive when there were signs or history of gonorrhœa. A positive reaction was often obtained in cases which were apparently cured. Schwartz and McNeil consider that a positive reaction is evidence of the presence of a focus of active gonococci, and hence of an infectious condition.

It is noteworthy that a positive reaction was obtained in all cases treated with gonorrhœal vaccines. This seems to show that specific antibodies to the gonococcus are readily formed in the human body.

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CHAPTER XXVIII

MICROBIOLOGY AND EXPERIMENTAL SYPHILOLOGY

The *Spirochæta pallida* (or *Treponema pallidum*) has been found in practically all the lesions of syphilis, but not in those of parasyphilis. The spirochætes are especially numerous in the perivascular tissues, but are only occasionally found in the blood. They are more constantly present in the lymphatic vessels and glands. They have been found in the cerebro-spinal fluid in cerebro-spinal syphilis (Gaucher, Merle, and Neisser), in the saliva; and in the urine in cases of syphilitic nephritis. So far they have not been found in the semen, but are probably present, because the experiments of Finger and Landsteiner have shown that the semen is contagious. In gummata they are found in the peripheral parts, but not in the central necrosed tissue. In congenital syphilis the spirochætes are more diffusely distributed than in the acquired disease, and have been found in all the organs of the body, including the ovaries. Levaditi found them within the young ova in a child of one month born of a syphilitic mother. Hoffmann has also found them within the ova. This fact is in favour of the transmission of syphilis by infection of the ovum. They have been found by Levaditi and others in the umbilical cord and placenta, but only in the fœtal part of the latter. Baisch, however, claims to have found them in the maternal part of the placenta in cases of congenital syphilis, and therefore in the mother's circulation. In the experimental syphilis of monkeys they are found in the primary sore in anthropoid apes and lower monkeys, and in secondary papules and mucous patches, and also in the spleen, in anthropoid apes.

The *Spirochæta pallida* is therefore assumed to be the pathogenic organism of syphilis, although most attempts to cultivate this organism on an artificial medium outside the body have failed.

Culture Experiments. — Some experimenters, however, have recently reported successful cultivation of the spirochæte, and reproduction of the disease by inoculation in animals. Noguchi claims to have made pure cultures of the spirochæte, which, when inoculated into the testicles of rabbits, produced typical syphilitic lesions containing numerous spirochætes. The material used was testicular tissue of a rabbit previously inoculated with syphilis. The culture medium was serum water, from sheep, horse, or rabbit, to which a piece of sterile rabbit tissue was added. Sowade also reports successful cultivation of the spirochæte, and the production of general syphilis by inoculation.

Sporulation. — Several observers have recently described the phenomenon of 'granule shedding' in several varieties of spirochætes (Leishman, Andrew Balfour). The spirochætes discharge spherical granules, which enter the red corpuscles and develop in them, completing their cycle of evolution. This process is especially pronounced after an injection of salvarsan. Balfour has observed the phenomenon in the *Spirochæta pallida* after injection of salvarsan, and remarks that it is 'evidence of a protective nature on the part of the spirochæte. It is endeavouring to preserve itself from total extinction by expelling bodies which are undoubtedly resistant, and which may possibly be of the nature of spores.'

The occurrence of spore-formation will explain many points which are obscure in the life-history of the spirochæte. It is possible that the spirochætes exist in the form of spores in the latent periods of syphilis, and develop again into the spirochætal form on the occasion of certain conditions which favour their growth—conditions which probably signify diminished resistance on the part of the tissues of the host. In this way relapses and tertiary manifestations may be explained. It is also possible that spores are present in parasyphilis, in the lesions of which no spirochætes have been found; but it is

more probable that parasyphilis is due to the after-effects of the spirochætes on the tissues.

Incubation.—Before the appearance of the chancre histological changes can be seen in the tissues; these consist in an accumulation of lymphocytes and thickening of the endothelium of the vessels of the papillæ. The true incubation period is the interval between inoculation and the appearance of these changes. Levaditi, by experiments on monkeys and rabbits, has shown that this incubation period is not occupied by the spirochætes going through a cycle of evolution, but is due to their slow multiplication after transplantation to their new medium. When they become accustomed to the new medium they grow more rapidly and produce changes in the tissues.

Invasion of the Body.—The spirochætes appear to remain for a few hours in the lymph-spaces of the tissues at the point of inoculation, but that they soon afterwards extend into the surrounding tissues is shown by the fact that excision of the point of entry even eight hours after inoculation does not prevent the development of the chancre. From the point of entry they spread by the lymphatics to the lymphatic glands, where they undergo further multiplication, and then enter the general circulation. According to Levaditi, they also enter the bloodvessels from the point of inoculation. When the chancre appears, the spirochætes are already present in the blood and internal organs, as proved by Neisser's inoculations with the organs of syphilized monkeys. Hence the failure of excision of the chancre to prevent secondary symptoms. The spirochætes appear to have a predilection for the hæmatopoietic system, for the bone-marrow and spleen were the only internal organs of monkeys (apart from the testicle) which gave positive inoculations.

Phagocytosis.—The invasion of the tissues by the spirochætes is accompanied by the production of an abundance of mononuclear leucocytes. According to Metchnikoff, the spirochætes produce some substance which causes positive chemiotaxis of leucocytes, especially mononuclears, resulting in phagocytosis. Spirochætes have been seen within the phagocytes by Ehrmann and Schaudinn in acquired syphilis, and by

Levaditi in congenital syphilis. Levaditi also mentions the formation of granules (? spores) within the phagocytes.

Effect of Treatment on the Spirochæte.—Levy-Bing found that the spirochætes disappeared from syphilitic lesions after mercurial treatment, and the same has been reported after treatment with the new arsenical preparations. Other observers, however, have found them very persistent. Levaditi found spirochætes in a child whose mother had been treated with mercury during pregnancy. It is possible that both mercury and arsenic act by increasing the resisting power of the body, rather than by actually killing the spirochætes.

Biological Position of the Spirochæte.—The exact biological position of the *S. pallida* is not quite certain, but it is probably allied to the trypanosomes. Schaudinn found that certain trypanosomes (flagellated protozoa) produce spiral filaments resembling spirochætes. He therefore suggested that spirochætes were a variety of trypanosomes. MacLennan's observations, pointing in the same direction, have already been mentioned (p. 37). Krzyztalowicz and Siedlecki described what they thought to be stages of development in the spirochæte, with sexual union between large female and small male forms. These observations have not been confirmed, and the different forms they describe are not seen in congenital syphilis, where the *S. pallida* is free from mixture with other organisms.

Possible Variation of the Spirochæta Pallida.—It is an interesting question whether there is only one form of the *S. pallida* or several varieties. F. W. Mott suggests that, assuming the spirochæte to be a protozoon and the specific cause of syphilis, 'it is conceivable that there may be varieties of this organism, as there are of the malarial parasite or trypanosome.' He also thinks it possible that one of these varieties may have a special elective affinity for the nervous system, and cause general paralysis. There is considerable evidence in support of this view, both clinical and pathological. In the first place, another protozoon parasite, the *Trypanosoma Gambiense*, is known to have an affinity for the nervous system. Secondly, cases in which general paralysis or tabes occurred

in patients infected from the same source have been observed by Marie and Bernhard, Brosius, etc. In Brosius's cases, seven glass-blowers were infected one from another with chancre of the lips, and five of them afterwards developed tabes or general paralysis. This idea might be extended, for if there is a special variety of spirochæte with an affinity for the nervous system, it is conceivable that there may be other varieties which have affinities for other organs or systems of the body. However, this is at present hypothetical.

The question arises whether the cause of *malignant syphilis* and *phagedena* can be explained by a variation in the seed instead of in the soil—*i.e.*, by special varieties of the spirochæte. But the evidence is not in favour of this view, for it has been shown that the source from which malignant syphilis is contracted is not necessarily malignant itself; also that two persons may contract syphilis from the same source, and it may assume a malignant form in one but not in the other. Buschke and Fischer obtained normal primary sores by inoculation of monkeys with virus from malignant syphilis. Hence the cause of malignant syphilis probably lies in the soil. It is probable that syphilis tends to become malignant when implanted on a virgin soil. This view is supported by Colonel Lambkin's observations of syphilis among the natives of Uganda, showing that the disease is very malignant when it attacks a race previously free from the disease. Syphilization of a race for many generations tends to produce a milder form of the disease by inherited immunity.

There is no doubt that the different effects produced by syphilis in different persons are largely due to differences in the soil—*i.e.*, to the resultant of inherited and acquired conditions which have influenced that soil. Sir Jonathan Hutchinson remarks: 'Although it is admitted that a spirillum invasion is the first stage of syphilis, it would be a serious error if this parasite were regarded as representing the sum total of syphilis. From the first, the spirillum goes into a sort of partnership with the pre-existing tendencies of its victim.'

In this connection may be mentioned the spirochæte

(*Treponema pertenue*), almost identical with the *S. pallida*, found by Castellani in *yaws* or *parangi*, a disease which is regarded by some as a tropical form of syphilis. However, Castellani regards the two diseases as distinct for the following reasons: (1) A person with syphilis may contract yaws, and inversely. (2) Monkeys inoculated with syphilis are not immune to yaws, and inversely. (3) Syphilis is of worldwide distribution, while yaws is limited to the tropics. (4) Yaws existed in the Fiji Islands before syphilis was introduced. (5) The primary sore is almost always extragenital. (6) The lesions of yaws differ from syphilitic lesions in the absence of endo-periarteritis and giant cells, and in the presence of epidermic proliferation. Sir Jonathan Hutchinson, on the other hand, considers yaws as a *variant* of syphilis—framboesial syphilis. His arguments are as follows: (1) The spirochæte of yaws closely resembles the spirochæte of syphilis. (2) Yaws goes through three stages, like syphilis, and is curable by the same remedies. (3) The fact that a syphilitic subject can contract yaws is not conclusive, for syphilis may be contracted more than once, and the interval between the two infections may be very short. On the other hand, there is evidence to show that yaws, as a rule, does prevent syphilis. (4) Yaws is not confined to the tropics; sporadic cases and local epidemics have occurred in Europe—for instance, the epidemic which occurred among Cromwell's soldiers, known as *Sibbens* or *Frambæsia Cromwelliana*. These sporadic cases afterwards revert to the normal type of syphilis.

Sir Jonathan Hutchinson suggests that spirochætes bred in different climates and in different races may present slight variations. Hence the *S. pallida* may become modified according to the race or constitution of the host, may retain and transmit this modified form, and afterwards revert to the normal. This view is supported by the fact that in dark races there is a tendency to framboesial eruptions, even when syphilis is contracted from a European. In districts where yaws is prevalent framboesial eruptions often follow hard chancres on the genitals.

It is also noteworthy that a trypanosome (*T. equiperdum*)

has been found in *dourine*, a disease of horses which has certain resemblances to syphilis. In fact, Mott remarks that 'dourine may almost be regarded as the syphilis of equines,' for it is characterized by a primary sore on the genitals with lymphatic adenitis, followed by general infection of the blood and a papular eruption. Moreover, ataxic paraplegia sometimes occurs in dourine. In five of such cases, Mott found degeneration of the posterior roots and sclerosis of the posterior columns. He has also pointed out the similarity of the histological lesions of the nervous system in chronic trypanosome infections such as sleeping sickness and dourine to those of syphilis and parasyphilis — viz., perivascular infiltration of lymphocytes and plasma cells and hyperplasia of the neuroglia.

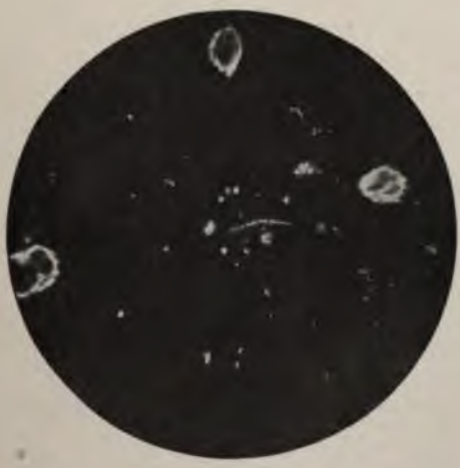
As Mott remarks, 'the study of these diseases is primarily biological. The *contagium vivum* is a living organism whose activities, like those of all living organisms, are for self-preservation and the preservation of the species.'

Further research on the life-history of the parasitic protozoa —the trypanosomes, spirochætes, etc.—may throw some light on the relationship of the diseases in which they are found.

New Methods of demonstrating the Spirochæte.—The method now most commonly used for demonstrating the spirochæte is that of dark ground illumination (incorrectly called by French authors the ultramicroscope). This method is by no means new, as many suppose, but is simply a revival of an old method used by microscopists more than fifty years ago. This method consists in the condensation of the lateral rays of light on the object by means of a parabolic condenser, the central rays being cut off by a diaphragm. A drop of cedar oil is placed between the condenser and the slide. Strong illumination is necessary, either electric or gas. The usual $\frac{1}{12}$-inch oil-immersion lens may be used; apochromatic lenses are not necessary. Under this illumination the spirochætes appear white on a black background (Plate VI.).

The *S. pallida* is distinguished from most other spirochætes by the following characters: (1) its diameter is small, $\frac{1}{4}$ μ, compared with its length, 10 to 15 μ; (2) it is very slightly refractile; (3) its ends are pointed, and often have

PLATE VI.



Spirochæta Pallida, with Dark Ground Illumination × 500.
(After Mucha)

To face page 494.

terminal filaments; (4) its spirals are deep and very regular, and it retains it spiral form under most conditions; (5) it colours red with Giemsa's solution; (6) its movements are slow, and consist of rotation on its axis, backward and forward progression, and lateral pendulum movements, the last being characteristic.

Other spirochætes, such as the *S. refringens* and *S. balanitidis*, which are also found on the surface of chancres and mucous patches, and the *S. buccalis*, found in the mouth, are thicker in proportion to their length, more refractile, and more variable in form. They have blunter ends and rarely terminal filaments, and the spirals are shallower and more irregular. Their movements are more rapid, but lateral bending is less marked. They stain bluish-red with Giemsa. The spirochætes which most resemble the *S. pallida* are the *S. dentium*, found in carious teeth; the *S. pseudo-pallida*, found in ulcerated cancers; and the *S. pertenuis* (*Treponema pertenue*) of yaws. The first and second have narrower spirals; the third differs very slightly from the *S. pallida*, but has flatter and more irregular spirals.

Material for examination should be obtained from the margin of lesions, and not from ulcerated areas, which contain other organisms. In the case of a chancre the surface should be cleansed with distilled water or saline solution and then rubbed with cotton-wool on a probe, or scraped gently with a blunt knife. The clear or slightly blood-stained exudation is then collected on a cover-glass and examined by dark ground illumination. Bleeding must be avoided, as the red corpuscles reflect the light and illuminate the field. Preparations may be ringed with vaseline for more prolonged examination.

Preparations may also be made from the affected lymphatic glands by puncture with a large hypodermic needle, after rendering the surface aseptic by tincture of iodine or other means. By squeezing the gland while the piston is withdrawn, a drop or two of exudation may be obtained. By this means spirochætes can sometimes be found when examination of the chancre is negative.

The Chinese Ink Method (*Burri*).—The secretion from the sore is mixed with equal quantities of a solution of Chinese ink and

distilled water, spread on a slide, allowed to dry, and examined by oil-immersion lens. The spirochætes appear white on a dark background. This method is simpler than that of dark ground illumination, but not so reliable, and obviously less suited for scientific observation.

Stained Preparations.—In addition to the methods described (see Appendix), the following may be mentioned:

1. *Preis's Modification of Giemsa's Method.*—Films are fixed and placed in 25 drops of Giemsa's solution to 10 c.c. distilled water, then heated over a Bunsen flame for a few minutes till vapour comes off. *S. pallida* stains dark red.

2. *Herxheimer's Method.*—Films are fixed in alcohol and stained for a quarter of an hour in hot gentian violet.

3. *Leishman's 'Serum' Method.*—Fix film in alcohol and cover with a drop of fresh blood-serum. Dry, and stain thirty minutes in equal parts of Leishman's stain and distilled water. The serum is said to intensify the stain. (Leishman's stain consists of an alcoholic solution of the precipitate obtained by mixing equal quantities of a 1 per cent. solution of methylene blue and a 1 in 1,000 solution of eosin.)

4. *Levaditi and Manouélian's Silver Nitrate Method for staining Sections.*—This is a modification of Levaditi's earlier method (see Appendix).

Fix small fragments of tissue in 10 per cent. formalin for twenty-four to forty-eight hours. Harden in alcohol 96 per cent. for twenty-four hours. Wash in distilled water till fragments sink. Place in following solution:

Pyridine	10 c.c.
Silver nitrate (1 per cent. solution in distilled water)	90 c.c.

Keep bottle hermetically sealed at temperature of room for two hours, then at 50° to 55° C. for three to five hours. Wash in distilled water, and place in reducing mixture for several hours:

Pyridine	17 c.c.
Acetone	10 c.c.
Pyrogallic acid (4 per cent. solution in distilled water)	90 c.c.

Dehydrate with alcohol, clear with xylol, imbed in paraffin, and cut into sections. Stain with polychrome methylene blue

or toluidine blue, and differentiate with glycerine ether. Spirochætes appear black, the tissues yellow.

5. Stern has applied the silver nitrate method to the staining of films. The latter are dried in air and kept for several hours at 37° C. They are then placed in 10 per cent. silver nitrate, and exposed to diffuse light for several hours. When they become brown they are washed and dried.

It may be mentioned here that the objections raised by Schulze and Saling, who regarded the spirochætes stained by silver nitrate as nerve filaments or elastic tissue fibrils, and called them 'silver spirochætes,' have been refuted by examination of the spirochætes in the living state and stained by other methods.

Experimental Inoculation.—The study of experimental syphilis in animals carried out by Metchnikoff and Roux has been continued by other investigators, especially by Neisser, Hoffmann, Finger and Landsteiner, and Levaditi. The results of these investigations have added considerably to our knowledge of syphilis, but, as Sir Jonathan Hutchinson has pointed out, it is necessary to exercise a certain amount of caution in applying these results to the human subject. Although monkeys and other animals can be inoculated with the syphilitic virus, they differ considerably in the absence of other constitutional conditions which affect the course of the disease in the human subject. In other words, the soil is different in animals and man.

Neisser's experiments on monkeys seem to show that there is not much variation in the virulence of the spirochæte, for the results of inoculation were the same with human and animal virus, with virus taken from acquired and congenital syphilis, and with virus from primary, secondary, and tertiary lesions. No diminution of virulence was observed, nor could it be produced by chemical or physical means, nor by syphilitic serum or by passage through animals. The only differences noted were in the incubation periods, which Neisser attributes to differences in the quantity of virus. He therefore thinks it is difficult or impossible to obtain a mitigated virus or vaccine for prophylactic purposes.

Neisser found that the internal organs of anthropoid apes (bone-marrow, spleen, and testicle) were infectious, although spirochætes are rarely found in them; also that these organs were infectious before the primary sore appeared, showing that general infection takes place rapidly. Moreover, he found that the internal organs of the lower apes were infectious, although these animals do not present external signs of secondary syphilis like the anthropoids. It is possible that this may also occur in man, and may explain cases in which syphilis is apparently limited to the primary sore—cases of apparent spontaneous recovery, several instances of which were collected by the late R. W. Taylor.

Inoculation of apes from recent human chancres and secondary papules is usually positive. Inoculation from tertiary gummata is also positive when the material is taken from the peripheral part of the gumma, but negative when taken from the central necrotic part. This agrees with the fact that spirochætes have been found in the peripheral parts of the gumma. The contagiousness of gummata, therefore, is limited to the early stages and the peripheral parts of the later stages, and ceases with gummatous degeneration of the tissues.

As regards the *blood*, Hoffmann, Finger and Landsteiner, have shown, by inoculating apes with blood from untreated cases of secondary syphilis, that the blood is contagious at certain periods, but not at others. This is in accord with the rarity with which the spirochæte is found in the blood. Hoffmann found that the blood of syphilitics may be infectious forty days after infection, before the appearance of the roseola. Neisser found the blood of two apes inoculated with syphilis to be infectious fourteen and eighteen days respectively after inoculation, showing that general infection was present before the chancre appeared.

The experiments of Finger and Landsteiner tend to confirm the view that the *semen* may be contagious. They successfully inoculated two apes with semen obtained by expressing the seminal vesicles of a patient with secondary syphilis. In another case a positive result was obtained by inoculating an ape with semen from a case of syphilis of three years' duration.

These observers conclude that the semen is always contagious in the secondary period, even when the testicles are apparently healthy; in tertiary syphilis only when the testicles are affected.

As regards the *cerebro-spinal fluid*, Hoffmann obtained a positive result by inoculating an ape with cerebro-spinal fluid from a case of secondary syphilis.

Finger and Landsteiner found that more positive inoculations and more typical chancres were produced in monkeys by inoculation of the virus in subepidermic pockets than by simple scarification. By this means a larger quantity of the virus could be introduced. This shows that the epidermis and the superficial layers of the dermis are the places of predilection for the pullulation of spirochætes. Inoculations into the subcutaneous tissue were negative. Levaditi explains this by phagocytosis being more active in the subcutaneous tissue than in the skin.

Inoculation of mucous membranes was negative when the virus was rubbed on an intact surface, but positive after scarification. This seems to show that a solution of continuity is necessary, and that the spirochætes are incapable of penetrating healthy skin and mucous membrane. Intraperitoneal inoculation was negative; but Neisser has reported a positive result from intravenous inoculation of an ape, with the production of general syphilis.

Syphilis in the Rabbit, etc.—Although the chimpanzee appears to be the only animal which, after inoculation with human syphilitic virus, presents symptoms similar, to a certain extent (tertiary lesions have not been observed), to those of human syphilis, modified forms of the infection have been produced in other animals, such as the rabbit, dog, cat, and guinea-pig.

In the rabbit, Bertarelli, by inoculation of the cornea with human virus, produced parenchymatous keratitis with spirochætes between the lamellæ of the cornea. From the cornea thus infected he was able to transmit the virus through a series of other rabbits, and also to inoculate guinea-pigs and monkeys. The rabbit has also been inoculated on the scrotum, with the production of an indurated chancre resembling a human chancre, and in the testicle, producing orchitis. No

symptoms of generalized syphilis were observed in these cases, but Schucht has reported the presence of spirochætes in the organs of rabbits inoculated in the cornea, and Neisser produced a chancre in a monkey by inoculation with the renal tissue of the infected rabbit. More recently, Grouven has reported the occurrence of generalized syphilis in the rabbit after corneal inoculation—papular eruptions containing spirochætes, serpiginous ulcerations, and spirochætes in the kidney and testicle. Sowade also reports the production of general syphilis in the rabbit by inoculation of pure cultures, the symptoms including papular eruptions, adenitis, and iritis.

Immunity.—Recent research has shown that immunity in syphilis is relative and not absolute, and that it depends on the presence of the active virus within the body.

During the first incubation period there is no immunity, and reinoculations are positive. During the primary period immunity is established slowly, and positive inoculations may be made up to twelve days after the first appearance of the chancre (Queyrat); up to thirty days (Pinard). During the secondary period the process of immunity reaches its maximum, but is even then not complete, for Finger and Landsteiner, by inoculation of virus into subepidermic pockets, found that most cases of syphilis showed local specific reactions, even during the presence of secondary eruptions. The same observers found that similar inoculations during the tertiary period gave rise to lesions of a tertiary nature. That these lesions were produced by the inoculated virus, and were not simply irritation reactions caused by the virus already present in the body, was proved by control inoculations with sterilized virus. Again, Neisser, by experiments on monkeys, showed that the internal organs are virulent and give rise to positive inoculations when the skin has acquired a definite degree of immunity.

Syphilitic immunity must therefore be regarded as 'a relatively refractory state of the skin and mucous membrane to external spirochætes, not complete immunity with absolute sterilization of the organism' (Levaditi). Further, this cutaneous immunity is probably confined to certain regions.

It does not begin till a certain time before the appearance of the secondary manifestations, increases progressively during the secondary period, diminishes during the tertiary period, but does not disappear altogether during this period, as shown by the character of the lesions produced by inoculation. Finger and Landsteiner found that tertiary lesions were similar whether produced by spirochætes within the organism or from without by inoculation. They produced gummas and serpiginous ulcers by inoculation of the virus from primary and secondary lesions, thus showing that the special characters of tertiary lesions do not depend on the quality of the virus, but on the mode of reaction of the tissues. Immunity is thus relative and regional, and can be overcome with a sufficient quantity of virus.

As regards the mechanism of immunity, this may be due to phagocytosis or to the formation of antibodies. Levaditi and others have shown that phagocytosis of spirochætes actually occurs, and Levaditi is of opinion that this process takes the chief part in immunity. Phagocytosis probably explains the negative results of subcutaneous as distinguished from subepidermic inoculations. As regards antibodies, although these have not been definitely demonstrated, by analogy with other spirilloses, such as tick-fever, they are probably present and take part in immunity. Levaditi suggests that antibodies are formed shortly before the commencement of cutaneous immunity, and persist during the disease, exerting a certain check on the growth of the spirochætes; but that when the latter become adapted to their environment they resist the action of the antibodies, and produce fresh lesions. This hypothesis explains the coexistence of immunity of the skin against external spirochætes with receptivity to internal spirochætes.

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CHAPTER XXIX

SERUM DIAGNOSIS

The Wassermann Reaction

In 1906, soon after the discovery of the *Spirochæta pallida*, Wassermann, Neisser, and Bruck applied the complement fixation test of Bordet and Gengou to the serum diagnosis of syphilis, with the result that syphilitic serum, in the majority of cases, was found to fix, or deviate, complement.

In order to understand this reaction, a few preliminary remarks on recent research in immunity are necessary. It appears that in all infective diseases substances are formed in the blood as the result of infection by micro-organisms. These substances are called *immune-bodies* or *antibodies*, and the micro-organisms or their products which give rise to them are called *antigens*. When antibodies have been produced in sufficient quantity to neutralize the antigen, immunity is established towards that particular antigen, but to that only, for the antigen and antibody have a specific relationship.

Ehrlich distinguishes three classes of antibodies. In the first class the antibody unites with the antigen without causing any change in it; this class includes the *antitoxins*. In the second class the antibody produces a physical change in the antigen, such as agglutination. In the third class the antibody combines not only with the antigen, but also with a substance, called *complement*, which is present in normal serum. To this class of antibody Ehrlich gives the name of *amboceptor*.

Antigens are not necessarily micro-organisms or their products, for the tissue cells of any animal, when introduced into

an animal of another species, act as antigens, and give rise to antibodies. Bordet and Gengou (1901) found that when the red corpuscles of a rabbit were injected into a guinea-pig, the serum of the latter acquired the power of dissolving them, a phenomenon known as *hæmolysis*. They also found that this phenomenon was due to the presence of two substances: (1) the antibody, or amboceptor, produced in response to the injection of the rabbit's corpuscles, or antigen; (2) the complement. The latter is destroyed by heating to 55° C. for an hour, but the antibody is not affected.

It was also found that amboceptors are produced by the injection of pathogenic organisms. In some cases this can be shown directly by their action on the antigen; thus, Pfeiffer showed that the serum of animals injected with typhoid or cholera bacilli acquired the power of dissolving the bacilli (bacteriolysis). In other cases the presence of the amboceptor can only be shown indirectly, by its power of fixing complement in conjunction with the antigen. This is demonstrated by adding a mixture of the red corpuscles of one animal and the serum of an animal of another species immunized against them. The corpuscles must be 'sensitized,' or washed, to free them from plasma, and the serum must be 'inactivated,' to destroy the complement contained in it. This mixture, together with fresh complement (usually obtained from the guinea-pig), is known as a *hæmolytic system*.

If the amboceptor is present in the serum to be tested, it unites with the antigen and complement, and fixes the latter, so that hæmolysis of the red corpuscles cannot occur, owing to the hæmolytic system being incomplete. If the amboceptor is absent in the serum to be tested, the complement is free to unite with the amboceptor in the hæmolytic system, and cause hæmolysis of the corpuscles. This phenomenon is known as the complement fixation (or deviation) test of Bordet and Gengou, which signifies that, when an antigen meets with its corresponding antibody, it has the power of fixing or deviating complement.

Technique.—In Wassermann's original method the *antigen* used was fresh extract of fœtal syphilitic liver, which contains

numerous spirochætes. The hæmolytic system consisted of inactivated serum of a rabbit immunized against the red corpuscles of a sheep, 'sensitized' sheep's corpuscles, and complement contained in guinea-pig's serum.

The Hæmolytic System.—Sheep's blood is first defibrinated by shaking it in a flask with glass beads, and then centrifugalized, to separate the corpuscles. The corpuscles are then washed in normal saline several times, to get rid of all traces of plasma. The washed corpuscles are then injected into the rabbit intravenously, or into the peritoneal cavity, at intervals of a few days. The rabbit's blood must be tested from time to time till complete hæmolysis occurs in a dilution of 1 in 100. The rabbit is then killed, and the serum is collected, diluted, and stored in flasks of 1 c.c. capacity. The serum is then inactivated by heating the flasks to 55° C. for half an hour, to destroy complement. The serum thus prepared may be kept for several months.

Complement is obtained by killing a guinea-pig, collecting its blood, and separating the serum. The latter is diluted with normal saline, according to its strength, which must always be ascertained beforehand, and should be used fresh, as it does not keep more than thirty-six hours.

The Antigen.—Liver from a case of congenital syphilis is minced, frozen, and ground to powder in a mortar, then dried *in vacuo* over sulphuric acid or anhydrous calcium chloride. The powdered liver, when required for use, is mixed with normal saline (1 gramme of powder to 30 c.c. of saline).

The blood to be tested may be obtained either by puncturing the end of the finger and drawing the blood into a pipette, or from a vein by means of a syringe. About 2 to 5 c.c. are required. The pipette is sealed, and the blood left to clot. It is then centrifugalized, and the serum drawn off by a graduated capillary pipette. The latter is sealed and heated in a water-bath at 55° C. for half an hour, to inactivate it (destroy complement).

Seven test-tubes are now required—one for the reaction, the others for controls. The controls must show—(1) that the hæmolytic system is active; (2) that the liver extract alone

does not fix complement and so prevent hæmolysis; (3) that the liver extract, together with the inactivated serum from a known case of syphilis, fixes complement and so prevents hæmolysis; (4) that the inactivated serum to be tested does not fix complement alone. To test the hæmolytic system two tubes are necessary—one to show that inactivated serum and complement causes hæmolysis, the other that the serum alone does not. The tubes are charged as follows:

No. 1 contains 0·1 c.c. of complement (diluted 50 per cent.).

No. 2 contains 0·2 c.c. liver extract + 0·1 c.c. complement.

No. 3 contains 0·2 c.c. liver extract + 0·2 c.c. serum to be tested + 0·1 c.c. complement.

No. 4 contains 0·2 c.c. patient's serum + 0·1 c.c. complement.

No. 5 contains 0·2 c.c. known syphilitic serum + 0·2 c.c. liver extract + 0·1 c.c. complement.

No. 6 contains 0·2 c.c. non-syphilitic serum + 0·2 c.c. liver extract + 0·1 c.c. complement.

No. 7 contains 2 c.c. of normal saline only.

Each tube is made up to 2 c.c. by adding normal saline. All the tubes are then incubated at 37° C. for one and a half hours.

The next step is the addition of the hæmolytic system, enough to supply 1 c.c. to each tube—*i.e.*, 7 c.c. of a mixture consisting of equal parts of a 5 per cent. suspension of sheep's corpuscles in normal saline and inactivated rabbit's serum. All the tubes are then again incubated for half an hour. It will then be found that hæmolysis has occurred in Nos. 1, 2, 4, and 6 of the control tubes, but not in No. 7, because of the absence of complement. In No. 5, containing known syphilitic serum, there is no hæmolysis, because the antibody in this serum has fixed the complement. As regards tube No. 3, containing the serum to be tested, if hæmolysis has occurred, the serum is non-syphilitic; if there is no hæmolysis, the corpuscles sinking to the bottom of the tube, the serum is syphilitic. In other words, hæmolysis signifies a negative reaction, absence of hæmolysis a positive reaction.

Modifications of the Test.—Various modifications have

been made in the original technique, the chief of which concern the antigen. In the original method fresh extract of syphilitic liver was used, but as this did not keep long, and could not always be obtained when required, an alcoholic extract was used. This in itself shows that the antigen does not depend on the presence of living spirochætes. It was afterwards shown that extract of non-syphilitic liver or other organs, such as the heart, would act as antigen ; further, that certain chemical substances belonging to the class of lipoids, such as lecithin, cholesterin, etc., would also act as antigen. This point will be referred to later. Most workers now use extract of mammalian heart or liver as antigen. However, according to Plaut and most other authorities, the results are more reliable when syphilitic tissues are used.

Several workers have devised further modifications of the test with a view to simplify it. Thus, instead of an anti-sheep hæmolytic system, an antihuman system—*i.e.*, rabbit's serum immunized against human corpuscles—has been used. According to Yamanouchi, this is a more delicate method, because human serum contains a natural antibody or amboceptor to sheep's corpuscles, which may sometimes cause hæmolysis, or a negative result, when syphilis is present. Bauer made use of the presence of this natural antibody for sheep's corpuscles in human blood for another modification. Hecht went a step further, and used the natural complement present in human serum, thus dispensing with the preliminary inactivation of the serum to be tested. Fleming has introduced another method similar to Hecht's, but with modifications in detail. Noguchi devised filter-papers impregnated with the antigen, amboceptor, and complement, which would keep well, and could be rendered active by soaking in normal saline.

It is unnecessary to give further details of these modifications, as the most experienced workers now agree that the original technique is the most reliable, because with all modifications positive reactions may be obtained in non-syphilitic cases, so variable is the complement and natural antibody for sheep's corpuscles in human serum. Moreover, the modifications cannot be used quantitatively.

Quantitative Test.—The test as carried out originally is qualitative only, but more recent investigations have shown that complement deviation might be produced under certain conditions by the different reagents used in the test. Thus, Browning and McKenzie and Noguchi showed that liver extract alone contained substances which would deviate complement, and therefore that these substances must be got rid of before the liver is used for antigen. Candler dissolves these substances in acetone previous to making the alcoholic extract. Browning and McKenzie found that different samples of guinea-pig's serum varied in degree of complement fixation. It was also found that a turbid emulsion of liver extract fixes more complement than a clear extract. Lastly, it was shown that non-syphilitic serum, when unheated, may cause complement deviation. Hence it became necessary to determine, not merely the occurrence of complement fixation, but the actual amount fixed—in other words, to institute a quantitative test.

McDonagh remarks that in a quantitative test either the amount of complement capable of being fixed by a given serum, or the amount of antibody in a given serum, may be determined. Boas has shown that the latter method is more delicate than the former. It is carried out by employing varying strengths of serum. According to McDonagh, the object of a quantitative test is to be able to estimate the influence of treatment. The substance responsible for a positive reaction is called 'reagin,' and this is said to diminish as a result of treatment. Since it is the presence or absence of 'reagin' that we wish to determine, it is better to find the quantity present than to estimate the fixing power of a foreign substance.

Nature of the Reaction.—The fact that an alcoholic extract of syphilitic liver would produce the reaction first showed that the effect does not depend on the presence of living spirochætes. This fact was further emphasized by the power of extracts of non-syphilitic organs to act as antigens. Thus, the serum reaction in syphilis is not a true antigen antibody reaction in the original sense of the term, and does not conform with the phenomenon of bacteriolysis.

The discovery that bodies of a lipoid nature,* such as lecithin, cholesterin, etc., would act as antigens then led to the idea that the reaction might be due to excess of lipoid substances in the serum of syphilitic patients, produced indirectly by the action of the spirochætes. As lipoids are present in normal tissues, the difference between syphilitic and non-syphilitic serum must therefore be quantitative and not qualitative. Porges and Meier showed that a flocculent precipitate was formed by the addition of lecithin to serum, and that this was greater with syphilitic than normal serum.

Levaditi and Yamanouchi suggested that certain compounds of the nature of cholesterin are present in the serum, and that these, in the presence of lipoids, are able to fix complement. According to this view the deviation of complement is due to the presence of two kinds of lipoids, and the reaction is caused by substances of histogenetic and not bacterial origin, resulting from tissue changes caused by the present or past action of the spirochætes.

Mott considers it probable that the syphilitic virus 'excites an increased unloosening of complex lipoid substances, containing lecithin and cholesterin, etc., from the red corpuscles and cells of the body.'

Results of Wassermann Test.—As a rule the reaction does not appear till some time after the appearance of the chancre—fifteen to thirty days according to Levaditi, but Lesser is said to have obtained a positive reaction in one case fourteen days before the chancre appeared. It appears that it takes some time for the antibodies to be formed which produce the reaction. In secondary syphilis the percentage of positive reactions is about 98, in tertiary syphilis 75, in latent syphilis 50. On the whole, about 85 per cent. of cases of active syphilis are said to give a positive reaction. In general paralysis it appears that the percentage of positive reactions is even higher than in active syphilis, a point which will be referred to later. Thus, the figures given for general paralysis are 100

* The term 'lipoid' is given to fat-like substances which are contained in all animal and vegetable cells. The best-known examples are lecithin and cholesterin.

per cent., and for tabes 50 to 70 per cent. by different observers. Further, in these cases the cerebro-spinal fluid usually gives a positive reaction as well as the serum, while in cases of active syphilis the cerebro-spinal fluid is usually negative.

On the other hand, cases with undoubted symptoms of syphilis sometimes give a negative reaction. In 1,000 cases examined by Blaschko, 70 with evidence of syphilis gave a negative reaction, including 36 with obvious syphilitic lesions. The occurrence of a negative reaction in cases with manifest syphilitic symptoms has been explained by Ehrlich and others by assuming that the spirochætes are encapsuled and thus cut off from the general circulation, so that they are unable to circulate the toxins which give rise to the antibodies which cause the reaction. The fact that spirochætes do become encapsuled has been demonstrated by Ehrmann and Levaditi. Another possible explanation is the existence of the spirochætes in a resting or spore stage, in which they would be still more unlikely to discharge toxins.

This brings us to the question whether a positive reaction necessarily signifies the presence of active spirochætes, or even the presence of spirochætes at all. Browning and others incline to the opinion that it does, even in parasyphilitic affections. But the histological evidence does not support this view, for spirochætes have, so far, not been found in parasyphilitic lesions; yet cases of parasyphilis (at any rate general paralysis) give a higher percentage of positive reactions than do cases of active syphilis. In other words, the reaction is more often positive when spirochætes are apparently absent. This seems to indicate that the reaction is not dependent on the presence of spirochætes, at any rate in the active stage. It is true that they may be present in a spore stage, but it seems more probable that the biochemical changes which cause the reaction, though originally due to the action of spirochætes, may continue independently of the presence of these organisms, even after they are all dead.

In *congenital syphilis* the reaction is usually positive. Leroux and Labbé, who have recently studied the subject of heredo-

syphilis at the Fortada-Heine Dispensary, Paris, find that the reaction is nearly always positive in cases of virulent early heredo-syphilis, and in 85 per cent. of cases of late heredo-syphilis. They also found that 71 per cent. of the mothers of heredo-syphilitic infants gave a positive reaction, whether they had signs of syphilis or not. Similar results have been obtained by other observers.

The fact that the majority of the mothers of heredo-syphilitic infants give a positive Wassermann reaction, even when they show no clinical evidence of syphilis, may be explained in three different ways: (1) The mothers may be affected with latent syphilis, due to actual foci of spirochætes; (2) the complement-binding substance which produces the positive reaction may be derived from the fœtus and pass through the placenta into the maternal circulation without causing actual syphilis; (3) the mothers may be immunized, if the complement-binding substance in the maternal circulation is of the nature of an anti-toxin. Baisch, by combined serological and bacteriological investigations, comes to the conclusion that the first of these explanations is the correct one, for the following reasons: (1) He found spirochætes in the maternal part of the placenta (in the decidual tissue and intervillous spaces); (2) the reaction remains positive several months after the birth of the infant; (3) the reaction may be different in mother and infant: sometimes it is negative in the mother and positive in the infant, and inversely. According to Baisch, this signifies that the complement-binding substance is formed in the organism in which it is found, and does not traverse the placenta. Leroux and Labbé consider that maternal syphilis is more often derived from the fœtus (conceptional syphilis) than by direct infection from the father. They also state that if a father with active syphilis and a positive reaction procreates a syphilitic infant with a positive reaction, the mother always gives a positive reaction. According to this view, Colles' law (p. 323) is explained by the mothers of heredo-syphilitic infants being themselves actually syphilitic, although the disease may remain latent for a long time.

On the other hand, clinical evidence seems to show that

some at least of the mothers of syphilitic infants may escape infection. Hochsinger has followed up the histories of seventy-two families in which the fathers were syphilitic, but the mothers showed no signs of syphilis during periods of four to nineteen years, although they were repeatedly examined. The 72 mothers gave birth to 276 syphilitic children.

Specificity of the Reaction.—The Wassermann reaction is not absolutely specific for syphilis, for it has been obtained in other diseases. The chief of these are other protozoal diseases, including sleeping-sickness, yaws, and malaria; in fact, the reaction was at one time thought to be peculiar to protozoal diseases. However, it has been obtained in tuberous leprosy. It is also reported to occur after narcosis, and in non-syphilitic subjects just before or just after death. Apart from these conditions, it appears to be rare for positive reactions to be obtained in non-syphilitic cases. However, Major French has recently reported positive reactions in ten cases of non-specific chancre which did not develop syphilis, although mercury was withheld. The blood was tested at periods varying from one week to three months. These cases require further confirmation.

Diagnostic Value of the Reaction.—We have seen that the Wassermann reaction in syphilis is not a true antigen antibody reaction in the sense that Bordet and Gengou described. We have seen that the reaction occurs in other diseases than syphilis. We have seen that the reaction is quantitative and not qualitative, depending on differences in degree, rather than in kind, in the sera of syphilitic and non-syphilitic subjects. We have also seen that cases with definite syphilitic lesions may give a negative reaction. Yet those who have had most experience with the test, chiefly pathologists, regard it as for all practical purposes specific for syphilis. Whether this is a logical or scientific standpoint is open to question.

From the clinical and practical standpoint it is important to know how far the Wassermann test will help us in the differential diagnosis between syphilitic and non-syphilitic lesions. Now, even assuming that the reaction is specific

for syphilis, a positive reaction does not prove that the lesion in question is syphilitic. It may be a non-syphilitic lesion occurring in a subject who has previously been infected with syphilis. Further, if we accept the most recent explanations of the nature of the reaction, a positive result does not necessarily show the presence of active syphilis, for, according to the lipoid theory, the reaction is due to tissue changes, which may persist after all the spirochætes are dead. As Candler remarks, 'a positive serum reaction merely indicates that the patient has had syphilis.'

It is obvious that grave errors in diagnosis may be made if too much reliance is placed on the result of the Wassermann reaction. For example, in diagnosing between syphilis and epithelioma of the tongue, it is very likely for the patient to give a positive reaction, for syphilis is a well-known predisposing cause of cancer of the tongue; yet this reaction does not exclude epithelioma, and hence does not help us in diagnosis. On the contrary, it may lead to useless treatment and the loss of valuable time by postponing operation. The same error may occur in many other instances where the reaction is appealed to to settle the diagnosis between syphilitic and non-syphilitic lesions.

On the other hand, there is evidence to show that the Wassermann reaction is of value in distinguishing between syphilitic and parasyphilitic affections of the nervous system, especially between cerebro-spinal syphilis and general paralysis and tabes, and also between general paralysis and other forms of insanity. In cerebro-spinal syphilis the serum often gives a positive reaction, the cerebro-spinal fluid very rarely. In general paralysis and tabes, however, the cerebro-spinal fluid gives a positive reaction in the majority of cases. Plaut obtained a positive reaction in the cerebro-spinal fluid in general paralysis in 96 per cent. of his cases, and 64 per cent. in tabes. This test is, therefore, of value in differentiating between cerebro-spinal syphilis and early cases of tabes and general paralysis. A good example is given by Mott: a case with all the signs of early tabes—lightning pains, girdle pains, paræsthesia of lower limbs, loss of knee jerks, and sluggish

pupil reaction to light—gave a negative reaction with the cerebro-spinal fluid. This case recovered under mercurial inunction, and was probably one of pseudo-tabes.

According to Mott, in tabes and general paralysis the central nervous system, which is normally protected against loss of lipoid substances, takes part in the bio-chemical processes induced by the syphilitic virus, and discharges lipoids into the cerebro-spinal fluid.

It is useful to combine the evidence of the Wassermann reaction with that of lymphocytosis of the cerebro-spinal fluid. Candler considers that lymphocytosis indicates organic disease of the central nervous system, but not necessarily syphilis or parasyphilis. But lymphocytosis, together with a positive Wassermann reaction of the cerebro-spinal fluid, points to general paralysis rather than to cerebral syphilis.

From the above considerations it seems reasonable to conclude that, although the Wassermann test is useful in the diagnosis of certain affections, chiefly of the nervous system, its value in the differential diagnosis of syphilitic and non-syphilitic lesions, as a whole, has been exaggerated. Laboratory tests are useful when used in conjunction with clinical evidence, but they should never be allowed to supplant it.

Effect of Treatment on the Reaction.—Energetic mercurial treatment appears to transform a positive into a negative reaction, at any rate temporarily. Of the different methods of mercurial treatment, inunction is said to have the most marked effect on the reaction, and internal administration the least. On these grounds the reaction is regarded by some observers as a guide to treatment, both as regards methods and duration. Treatment, they say, should be continued till the reaction becomes permanently negative. However, several arguments may be urged against this view. In the first place, both in congenital syphilis and in general paralysis, the two classes of cases which give the reaction most constantly, the effect of treatment on the reaction is little or none. Secondly, as we have already mentioned, there is no proof that a positive reaction necessarily means the presence of active virus.

If the Wassermann reaction is specific for syphilis, it is best

to look upon it as indicating a previous infection. To regard it as evidence of virulent syphilis, and therefore an indication for active treatment, in a person with no signs or symptoms of the disease, is to attach far too great importance to its value. Clinical evidence should never be abandoned in favour of a laboratory test, especially when the actual nature of the changes on which the test depends is still obscure, and the reaction itself is subject to so many variations. For the same reasons, the reaction cannot be accepted as a test of the relative merits of different methods of treatment. Moreover, as Levaditi points out, it is possible that a positive reaction may be a reaction of immunity, analogous to agglutination, which may continue long after the cure of typhoid fever.

It cannot be too strongly emphasized that in the treatment of syphilis we should not depend on rules and regulations, but should be guided by the clinical symptoms. The disease varies so much in different patients that each case must be treated individually. We must treat not only the disease but also the patient, whether his Wassermann reaction is positive or negative. As Leroux remarks: 'La clinique reste seule maîtresse des indications diagnostiques, prognostiques, thérapeutiques.'

Cutaneous Reaction in Syphilis.

The production of a cutaneous reaction by Von Pirquet and others in tuberculosis suggested the application of this method to syphilis. For this purpose Nicolas, Favre, Gautier, and Chartet used a glycerine extract of the liver from cases of congenital syphilis, sterilized by heating to 115° C. To this extract they gave the name of 'syphiline.' Intradermic inoculation gave better results than cutaneous. The results were compared with those of the Wassermann reaction, and agreed (intradermic) in 42 out of 50 cases. In two cases of undoubted syphilis a positive intradermic reaction was obtained when the Wassermann test was negative. The 'syphiline' was prepared by trituration of dried congenital syphilitic liver in a mortar, and then heating with 10 per cent. bouillon-glycerin at 115° C. for fifteen minutes. It is then

filtered, reduced by evaporation at 65° C., and diluted with two parts of serum. One drop of this is used for injection.

The above observers also tried the cutaneous and intradermic injection of tuberculin in syphilitic subjects, and came to the remarkable conclusion that syphilitics react to tuberculin in the same proportion as do tuberculous subjects.

More recently Fontana has experimented with different substances, with the object of producing a cutaneous reaction. He tried 'syphiline' prepared from condylomata, extract of guinea-pig's heart, sodium glycocholate, and a preparation of lecithin. The only one of these which gave satisfactory results was 'syphiline.' This was tried in 67 cases, 51 syphilitic and 16 non-syphilitic. Of the 51 syphilitics, 27 gave a positive reaction after 24 hours, consisting in true infiltration of the skin, while in the non-syphilitic cases only 2 reacted. The results compared with the Wassermann test were in favour of the latter, but Fontana thinks that with improved technique the syphiline test may give better results in the future.

Wolff-Eisner says: 'It now seems probable that this method may in the future be applied in preference to the Wassermann reaction. This hope is based on the fact that a syphilitic responds to an inoculation with extract of syphilitic material—*i.e.*, an antigen, with a reaction differing so greatly from that shown by a non-syphilitic as to be unmistakeable. In order that this method may be safely applied it is necessary that the antigen be so prepared that, without loss of activity, it will hold no danger for a non-syphilitic; in other words, to obtain a syphilitic extract which is killed, so that there is no danger of infection, and yet so carefully prepared that it loses nothing in efficacy.'

Further research is required to show whether a reliable cutaneous test can be obtained in syphilis. At any rate, such a test would have the advantage of simplicity.

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CHAPTER XXX

THE ARSENICAL TREATMENT OF SYPHILIS

ARSENIC has for a long time been used as an auxiliary medicament in the treatment of syphilis, chiefly in the form of Donovan's solution which contains iodides of arsenic and mercury, Fowler's solution, or liquor arsenicalis, and liquor sodii arseniatis. During the last few years, however, attempts have been made to exalt the therapeutic position of arsenic to that of an alternative drug to mercury, or even a substitute for it. To attain this object, several organic preparations have been constructed, for which it is claimed that larger quantities of arsenic can be administered with less toxic effects than is the case with the inorganic preparations.

The chief of these new preparations of arsenic are *atoxyl*, *arsacetin*, *hectine*, *arseno-phenyl-glycin* and *dioxy-diamido-arseno-benzol*.

Atoxyl (sodium-paramino-phenyl-arsenate).—This drug is said to have been introduced by a French chemist, Béchamp, more than fifty years ago. It was used in skin affections, but abandoned owing to the toxic effects of impurities, which sometimes caused blindness. More recently it was found to have a destructive effect on trypanosomes, and was hence tried in sleeping sickness. When the pathogenic microbe of syphilis (the *spirochæta pallida*) was found to be probably a protozoon, and therefore allied to the trypanosomes, atoxyl was also tried in syphilis. However, atoxyl has again been abandoned owing to the numerous cases of optic atrophy which have resulted from its use, both in sleeping sickness and in syphilis. Many cases of optic atrophy following the use of atoxyl in sleeping sickness in Koch's expedition have been reported (*Bulletin of*

the Sleeping Sickness Bureau, 1909). After this, Uhlenhuth introduced a combination of atoxyl with mercury, called *atoxylate of mercury*.

Arsacetin (sodium-acetyl-paramino-phenyl-arsenate).—This substance was introduced as a substitute for atoxyl, with the idea that it was equally efficacious and free from the danger of causing optic atrophy. However, cases of optic atrophy have resulted from its use, so that this drug has shared the fate of atoxyl.

Hectine (sodium-benzo-sulpho-paramino-phenyl-arsenate).—This preparation, introduced by Mouneyrat, has so far escaped the opprobrium which led to the abandonment of atoxyl and arsacetin. Hallopeau has stated that syphilis can be aborted in the earliest stage by daily injections of hectine for thirty days underneath and in the neighbourhood of the chancre, provided the latter is not more than twenty days old. However, this claim has not been confirmed by the results of other observers, including Augagneur and Moutot who reported several cases in which secondary syphilis followed in due course after abortive treatment carried out according to Hallopeau's instructions. Nevertheless, if there is no evidence that syphilis can be aborted or cured by hectine, this preparation undoubtedly has the advantage over other organic preparations of arsenic, insomuch as it has so far caused no deaths and no optic atrophy.

We now come to the latest of the new arsenical preparations—*arseno-phenyl-glycin* and *dioxy-diamido-arseno-benzol*, otherwise known as '606.' These preparations are the result of Ehrlich's experiments in chemo-therapy, carried out for a number of years in conjunction with Bertheim and Hata. Although opinions differ as to the ultimate benefit to be derived from such preparations in the case of human syphilis, there is good evidence of their curative action in certain other infections caused by similar parasites.

Ehrlich's Experimental Chemo-therapy.—Starting with the idea that drugs only act on an organism when they enter into chemical combination with its cells, Ehrlich applied his 'side-chain' theory to the action of drugs on the parasites of

infective diseases, especially those caused by the protozoal parasites, the trypanosomes and spirochætes. He assumed that the protoplasm of the parasite possesses certain specific 'receptors,' called 'chemoceptors,' which combine with the drug, and thus lead to death of the parasite. His object was to find a drug which would produce this *parasitotropic* effect without entering into combination with the cells of the host, and thus produce an *organotropic* or toxic effect. He experimented both with certain aniline dyes and with compounds of arsenic, but found that the former were too organotropic.

Turning his attention to the organic arsenical compounds, for the reason that atoxyl had been found to produce an effect on the trypanosomes of sleeping sickness, he found that only those compounds with a trivalent molecule possessed chemoceptors (*arsenoceptors*).

Atoxyl is pentavalent, but is split up in the body into both trivalent and bivalent molecules; the former have a parasitotropic effect, but the latter are organotropic, and produce the toxic effects, such as optic atrophy, which led to the abandonment of this drug. Atoxyl having been found to be an amido derivative of phenyl arsenious acid, this group was studied further by Ehrlich and Bertheim, and several hundred preparations were made, most of which failed to satisfy the requisite conditions. Eventually, arseno-phenyl-glycin, and soon afterwards dioxy-diamido-arseno-benzol were produced, the last being the six hundred and sixth preparation, and hence known as '606.' These two preparations were found to have the maximum parasitotropic with the minimum organotropic effect, but arseno-phenyl-glycin was soon superseded by '606.' Hata found that the latter killed the parasites of recurrent fever in mice in twenty-four hours, without producing any toxic effect, and in the spirillosis of chickens it was found more effective than atoxyl, arsacetin, atoxylate of mercury or arseno-phenyl-glycin.

'606' was next tried in the experimental syphilis of rabbits. The rabbit can be inoculated with syphilis in three different ways: in the cornea, producing parenchymatous keratitis; in the testicle, causing orchitis; and in the scrotum, giving rise to

an indurated sore, resembling a human hard chancre. After injection of '606' keratitis was rapidly cured, spirochætes disappeared from the chancre in twenty-four hours, and the sore healed in two or three weeks, and orchitis subsided. The Wassermann reaction was positive before, but negative after the injection.

The next step was to try '606' in human syphilis, but here there were difficulties. First of all it was impossible to find the maximum dose tolerated which is required to fulfil Ehrlich's ideal of *therapia sterilisans magna*, or dose which will destroy all the parasites without injuring the patient. Secondly, there was the difficulty of the hypersensibility to arsenic possessed by some individuals.

The drug was first tried by Alt in cases of general paralysis. Although little improvement was effected, the Wassermann reaction became negative in some cases. At any rate it was found that a dose of 0·3 gramme was well tolerated. It was then tried by Schreiber in cases of early syphilis with apparently good results. Wechselmann then used it extensively at the Rudolf Virchow Hospital in Berlin and published the results of 1,400 cases, comprising all stages and forms of syphilis, a large number of which had received no mercurial treatment. In 1911 '606' was patented and sold under the name of 'Salvarsan.'

Methods of Administration.—Salvarsan may be administered by subcutaneous, intramuscular, or intravenous injection. The two first methods are simpler but more painful, and liable to cause necrosis, even with the strictest antiseptic precautions. The intravenous method is now being more generally adopted, and has the advantage of causing less pain. It is, however, a more formidable operation and requires a more elaborate technique.

The earlier preparations of '606' were dissolved in methyl alcohol, but the latter is objectionable on account of its toxic effects, which may be due to impurities. The present form of the drug, salvarsan, is soluble in water and in caustic soda. The preparation itself is acid, but as an acid solution is extremely painful and also dangerous for intravenous injection,

the solution must be rendered alkaline or neutral. The more neutral the preparation the less the pain.

Subcutaneous and Intramuscular Injection. — The apparatus required is a large syringe of 20 c.c. capacity, provided with a platinum-iridium needle, the size of that of an exploring syringe. Strict antiseptic precautions are necessary. Injections may be made into the glutei or trapezius muscles.

1. *Alt's Alkaline Solution.*—The dose of salvarsan is placed with 10 c.c. of distilled water in a graduated glass cylinder of 100 c.c. capacity with a glass stopper, and shaken up with glass beads till a clear solution is obtained. Caustic soda is then added in the proportion of 0·5 c.c. to each 0·1 gramme of salvarsan, and the mixture shaken up for half a minute.

2. *Wechselmann's Neutral Emulsion.* — The salvarsan is dissolved in 1 or 2 c.c. of caustic soda in a mortar, then glacial acetic acid is added drop by drop till a yellow precipitate forms; 1 or 2 c.c. of sterile water are then added. The liquid is neutralized by $\frac{1}{10}$ normal caustic soda or 1 per cent. acetic acid, according to the reaction shown by litmus paper. The emulsion thus produced is centrifuged and the sediment taken up with physiological salt solution.

3. *Michaelis Neutral Suspension.*—From 0·3 to 0·6 gramme of sodium hydrochlorate is dissolved in 16 c.c. of hot sterile water in a wide graduated cylinder of 50 c.c. capacity. The salvarsan is then added and the mixture stirred with a glass rod till dissolved. From 3 to 5 c.c. of normal caustic soda are then added and the mixture stirred again. Three drops of a 0·5 per cent. alcoholic solution of phenolphthaleïn are added as an indicator, and then acetic acid till the phenolphthaleïn is dissolved. A yellow suspension is formed. After adding a few drops of caustic soda the suspension is ready for use.

4. *Citron's Method.*—The salvarsan is emptied into the barrel of a Record syringe of 15 c.c. capacity, and is moistened with a few drops of alcohol. Five c.c. of hot sterile water are added, and the piston of the syringe inserted. The syringe is shaken till a yellow solution is obtained. The piston is then removed and 40 drops of a 10 per cent. mixture of potassium

bicarbonate in physiological salt solution are added. A creamy emulsion results.

5. *Kromayer's Method.*—In this method the drug is made into an emulsion with liquid paraffin containing 0·1 gramme salvarsan to 1 c.c. Kromayer used this for out-patients, in doses of 0·1 or 0·2 gramme.

In making intramuscular injections care must be taken to avoid penetrating a vein. The needle should be inserted first to see if blood comes, before attaching syringe.

Emulsions are less painful than solutions of salvarsan, but less quickly absorbed and more likely to cause encapsuled deposits of the drug in the tissues.

Intravenous Injection (*Schreiber's Method*).—From 10 to 20 c.c. of sterile warm water are placed in a graduated cylinder of 250 c.c. capacity, with a glass stopper. The salvarsan is then added, and the mixture shaken till a clear solution results. Sterile water or physiological salt solution is added up to 100 c.c. Then 0·7 c.c. of normal caustic for each 0·1 gramme of salvarsan is added, and the mixture shaken till the precipitate formed is dissolved, and a clear solution results. Sterile water is added up to 200 c.c., and the solution decanted into a beaker for use.

McDonagh gives the following directions: Dissolve the salvarsan in 3 or 4 ounces of warm physiological salt solution in a graduated measure. When dissolved, add 10 c.c. of 0·8 per cent. caustic soda (normal caustic soda is 4 per cent.), and dissolve the resulting precipitate by further addition of caustic soda solution (about 7 c.c.). This should be added slowly and stirred well. The weak solution of caustic soda avoids the risk of making the solution too alkaline. When the solution is quite clear add saline solution up to 10 ounces.

Intravenous injection may be performed either by transfusion or by injection. The latter is to be preferred, because it is easier to manage and more under control. The amount of solution injected should not be more than 9 ounces (about 250 c.c.). Schreiber uses a bayonet-shaped needle with a three-way stop-cock, enabling the solution to be aspirated from the beaker and injected directly into the vein. Two beakers

are required—one containing the salvarsan solution, the other physiological saline. The syringe is all glass and of 20 c.c. capacity, and is connected with the stop-cock by means of a metal fitting. As the whole apparatus was rigid, and any movement dislodged the needle from the vein, McDonagh made some modifications which greatly facilitate the operation: (1) A movable joint in front of the stop-cock, so that any movement is broken at this joint, and not transmitted along to the needle; (2) a bayonet catch for the needle; (3) a rubber connection for the syringe. The syringe is filled with saline solution, and all air expressed from the apparatus. The needle is then inserted into the vein (previously made prominent by a rubber tourniquet) and fixed with the stop-cock open. If the needle is in the vein, as shown by blood entering the syringe, the tourniquet is loosened and some normal saline injected. If this causes infiltration, showing that the needle is not completely within the vein, the needle must be withdrawn and the operation repeated on another vein. If no infiltration occurs, the salvarsan solution is let into the syringe and injected, followed by more saline to avoid leaking of the salvarsan into the tissues. The solution must not be too concentrated and must be injected slowly. The patient should be kept in bed for a few days. The advantage of intravenous injection over intramuscular is the avoidance of possible deposits of arsenic in the tissues. The arsenic is said to be excreted in a few days, so that a second injection can be given after a short interval.

Dose.—The doses given for intramuscular injection vary from 0·3 to 0·6 gramme. Some observers have given 0·7 or even 1 gramme. The average dose for infants is 0·01 gramme. For intravenous injection, Ehrlich and McDonagh recommend 0·5 gramme for a man and 0·4 gramme for a woman. They also repeat the injection in five days in most cases, but not till after a month's interval in cases of nervous disease. A third injection is given in six weeks if the Wassermann reaction is positive. Leredde gives three injections of 0·6 gramme at intervals of eight days in primary syphilis; in secondary and tertiary syphilis four injections of 0·2, 0·4, 0·6, and 0·6 gramme

respectively. If there are active lesions of the nervous system he begins with 0·1 or 0·3 gramme, and gradually increases the dose if no bad effects ensue.

In syphilis of the nervous system McDonagh advises half the usual dose, as the reactionary inflammation may cause a rise of blood-pressure and inhibit the respiratory centre.

Results.—Wechselmann's results with salvarsan treatment are briefly as follows: In primary syphilis early chancres healed rapidly, but indurated chancres less quickly. The latter result was attributed to encapsulation of spirochætes in the indurated tissue, rendering them inaccessible to the action of the drug. Phagedenic chancres also healed after injection of salvarsan. In secondary syphilis the effect was rapid on lesions of the mucous membrane and condylomata. Good results were also obtained in periostitis, irido-cyclitis, and on syphilitic growths of the larynx. Improvement resulted in choroiditis, some cases of cerebral syphilis, and a few cases of interstitial keratitis. But the most marked effect was obtained in cases of malignant syphilis. In parasyphilis the results were less favourable. In tabes the lightning pains and gastric crises were improved temporarily, but sometimes recurred. In advanced cases there was no improvement. In ten pregnant women the drug was injected with no ill-effect on the child.

Results similar on the whole to Wechselmann's have been reported by many other observers, the most rapid and pronounced effects being produced in ulcerative lesions of the skin and mucous membranes, especially in cases of malignant syphilis.

Plaut and others have reported good results by using the serum of patients injected with salvarsan. Salvarsan is said to have a good effect on most affections of the eye of syphilitic nature, and some observers report temporary improvement in cases of interstitial keratitis.

As regards the possibility of aborting syphilis by injection of salvarsan in the early stages of the chancre, Ehrlich, Neisser, and Wechselmann, think this possible, and McDonagh states that six cases are on record in which the fact of abortion was

proved by reinfection. However, it is doubtful whether reinfection can be accepted as an absolute proof of the extinction of the first infection, for, as already mentioned, immunity in syphilis is relative and not absolute, and there is both experimental and clinical evidence to show that reinoculation may be positive before the first infection has died out. Moreover, it is not impossible that some cases of syphilis may undergo spontaneous abortion.

In *congenital syphilis* salvarsan has been tried both by direct and indirect methods. The direct method, by intramuscular injection, has caused the temporary disappearance of lesions, and favourable results have been recorded in cases of interstitial keratitis, but relapses have been frequent and several deaths have been reported.

It was suggested by Ehrlich that death of the infant after injection of salvarsan was due to the sudden liberation of endotoxins from the spirochætes killed by salvarsan. Such a supposition is purely theoretical; it is far more probable that death was due to arsenical poisoning or shock.

The indirect method consists in injecting the mother with salvarsan, and giving her the infant to suckle, on the supposition that either the drug itself or an antitoxin to which it gives rise in the mother is secreted in the milk. Cases in which the symptoms of congenital syphilis disappeared after this treatment have been reported by Taege, Duhot, Sequeira, and others, but failures necessitating recourse to mercurial treatment have also been published by Jeanselme, and deaths after such treatment by Kakels and Peiser.

The indirect method has been further extended, by injection of a goat with salvarsan and treatment of the syphilitic infant with the milk. Jesionek reported good results from this treatment. In his case a child of five years with acquired syphilis was treated with the milk of a goat injected with 40 centigrammes of salvarsan in the jugular vein. The symptoms in the child are said to have rapidly improved, and arsenic is reported to have been present in the goat's milk. However, this result has not been confirmed by the observations of Jeanselme, who treated an infant of five weeks with

congenital syphilis with the milk of a goat which had received seven injections of salvarsan (30 centigrammes for the first and 40 centigrammes for the other injections). In this case the symptoms improved slowly for a time, but then remained stationary, necessitating recourse to mercurial treatment. The goat's milk, when tested by Bougault's method, showed no trace of arsenic, and after comparison with milk containing a known quantity of arsenic, tested in the same way, led Jeanselme to the conclusion that the goat's milk, even if it contained any arsenic at all, could not have contained more than $\frac{1}{10}$ milligramme per litre, a quantity incapable of producing any therapeutic effect. Moreover, it is more than probable that any beneficial effect obtained by such treatment is due to the well-known nutritive qualities of the goat's milk itself, which was recommended in congenital syphilis by Fournier many years ago.

Recurrences.—It is impossible to estimate the proportion of recurrences after treatment by salvarsan, because such a large number of patients escape further observation. Wechselmann admits that the cases treated at Berlin were seldom seen again. He also mentions that out of 366 cases collected by Sieskund only 44 returned to the clinic, 8 of them with recurrences. It is obvious that two interpretations could be given of these figures by compilers of statistics, differing by a large percentage. Géronne published 300 cases, with 28 recurrences within six months, 6 of these after combined intramuscular and intravenous injections. Nicolas and Moutot found relapses frequent even after three or four injections of 0·6 gramme.

Combined Treatment with Mercury and Iodides.—Owing to the frequency of relapses, most authorities have abandoned the attempt to cure syphilis with salvarsan alone, and now recommend combined treatment with mercury and iodides. McDonagh and Fordyce give mercurial injections or inunctions in the intervals between intravenous injections of salvarsan. Nicolas and Moutot give prolonged mercurial treatment after two intravenous injections of salvarsan. Neisser recommends combined treatment with salvarsan ar

mercury. In tertiary lesions McDonagh gives iodides in addition to salvarsan. He also recommends excision of the primary sore when possible, or cauterization when this cannot be done.

As already mentioned, some observers are still of opinion that syphilis can be aborted by injections of salvarsan in the primary stage, but it seems a dangerous practice to rely upon this and abandon mercurial treatment, even if the Wassermann reaction remains negative.

Effect on Wassermann Reaction.—In the majority of cases the Wassermann reaction, previously positive, is reported to become negative, but this result is by no means constant, nor does it appear to be permanent. In 268 cases reported by Lange, the reaction became negative in four or five weeks in 153 cases; in 97 it remained positive. In the other 18 cases it was negative before the injection of salvarsan. Five of these were cases of tertiary syphilis which became positive after the injection; the remainder, comprising 1 case of tabes, 1 of malignant syphilis, 2 primary chancres, and 9 cases previously treated with mercury, remained negative. Two primary cases, previously negative, became positive after salvarsan, and 2 of the cases of tertiary syphilis, which became positive after salvarsan, became negative after a second injection. Géronne mentions 2 cases of primary syphilis in which the reaction became more positive in spite of several injections. It is, therefore, impossible at present to state the permanent effect of salvarsan on the Wassermann reaction.

Effect on the Spirochæte.—After an injection of salvarsan the spirochætes are said to disappear from the lesions in a few days, sometimes within twenty-four hours. When examined by dark-ground illumination their characteristic movements soon cease and they become swollen. Recently, however, Balfour has noticed the formation of granules, probably spores (see p. 489), after treatment by salvarsan, which would seem to indicate an effort at self-preservation. Hence the spirochætes may not be necessarily killed, but only forced to enter into another cycle of their life-history.

Dangers of Salvarsan.—Numerous accidents and a considerable number of deaths have resulted from the injection

of salvarsan, both by the intramuscular and intravenous methods. It is true that many of these unfortunate results may be explained by faults in technique and by injection in unsuitable or hopeless cases, but some of them appear to be due to the toxic action of the drug.

The accidents reported after subcutaneous and intramuscular injection include necrosis of skin and muscles, deposits of arsenic at the site of injection, and pulmonary embolism. These accidents may be avoided by the method of intravenous injection, provided it is skilfully performed and the injected fluid is absolutely clear, and not acid. But if the fluid contains solid particles there is danger of pulmonary embolism; if the fluid is acid, it may cause pulmonary thrombosis (Meissner); if it is too alkaline, it may cause local thrombosis of the vein; if it escapes into the tissues around the point of injection, it is liable to cause œdema and necrosis.

Toxic Effects.—Many unpleasant and sometimes alarming symptoms have been noted, especially after intravenous injection. These symptoms include fever, rigors, headache, vertigo, vomiting, diarrhœa, dyspnœa, œdema and cyanosis of the face, spasm of the diaphragm, clonic contractions of the muscles of the limbs, syncope, and collapse. Different interpretations of these symptoms are given by different authorities. Finger and others consider that they are due to acute arsenical intoxication. Ehrlich and Neisser attribute them to the setting free of endotoxins by the destruction of large numbers of spirochætes; but, according to Finger, similar symptoms are produced after injection of salvarsan in non-syphilitic cases, such as psoriasis and leprosy. Wechselmann suggests that these symptoms may be due to the presence of micro-organisms in the saline solution used for injection, which should be sterilized shortly before use. This explanation seems very improbable, for intravenous injections of saline solution have long been used in various conditions without causing these symptoms, and, as such injections are usually performed in cases of emergency, the saline solution is often not freshly prepared or sterilized. According to McDonagh, the collapse which sometimes occurs after intravenous injection is caused

by a sudden fall of blood-pressure, due to the solution being too alkaline.

As regards the frequency and severity of the above-mentioned symptoms, these differ in the reports of different observers. In Nicolas and Moutot's series of 318 intravenous injections, 122 caused no reaction, while 196 were followed by various degrees of reaction, including rise of temperature, rigors, vomiting, headache, diarrhœa, epigastric pain, albuminuria, retention of urine, and syncope.

In some cases toxic symptoms occur after a second or third injection, when the first has produced no ill-effects.

Whatever may be the explanation of the above immediate symptoms, there is considerable evidence that salvarsan has a toxic action on the nervous system and the kidneys, although here, again, there is a conflict of opinion.

As regards the *nervous system*, epileptiform convulsions, sometimes resulting in coma and death, have been reported by several observers (Hoffmann, Fischer, Kannengeser, Spiethoff, Hallopeau, Gaucher). In some cases the convulsions may have been of uræmic origin, as in a case reported by Gaucher, where the autopsy showed acute nephritis.

Affections of the *cranial nerves*, chiefly the motor oculi and the auditory, resulting in paralysis of certain eye muscles, labyrinthine deafness, and vertigo, have been reported by Finger, Stern, and others. Some hold that these lesions are syphilitic in nature and not toxic; others that they are due to the neurotoxic action of the drug; others, again, think that salvarsan causes a *locus minoris resistentiæ*, which predisposes the nerves to the action of the syphilitic virus. Ehrlich considers that these affections of the nerves are due to the survival of spirochætes in the bony canals after all the other spirochætes in the body have been destroyed by salvarsan. But there is no proof that all the other spirochætes are thus destroyed; on the contrary, Finger found that in several of his cases lesions of the skin and mucous membrane either coexisted with the nervous lesions or soon followed them. Finger also draws attention to the frequency of nerve lesions after treatment with salvarsan, as compared with their infrequency in

untreated cases and in cases treated with mercury, and regards the neurotoxic action of salvarsan as a contraindication to its use in the ordinary treatment of syphilis. McDonagh states that these nerve symptoms, which he calls 'neuro-recurrences,' usually disappear after a second injection or after mercurial inunction. Whichever view is correct, affections of the cranial nerves, especially the auditory, appear to have become more frequent since the introduction of salvarsan.

Buschke, who believes in the neurotoxic action of salvarsan, thinks it possible that microscopic foci of necrosis may be produced by deposits of salvarsan in the tissues of the internal organs, in the same way that deposits of the drug after intramuscular injection cause necrosis of the glutei muscles, and that these foci of necrosis may predispose to further manifestations of visceral syphilis. In support of this view he mentions the tendency of syphilitic eruptions to appear in tattoo-marks in the skin.

As regards *optic atrophy*, which was so frequent with atoxyl and arsacetin, the evidence as to salvarsan is not quite clear. Finger reported a case, but as this had been previously treated with atoxyl, arsacetin, and enesol, it is obviously uncertain which of the drugs was responsible. Isaac refers to two cases of blindness, and Starr mentions the case of a tabetic patient who became almost totally blind six weeks after an injection of salvarsan. These cases are also not conclusive. More recently, however, Nicolas and Moutot have reported one case of unilateral optic neuritis a month after the third injection of 0·6 gramme of salvarsan. Hence, we may conclude that if salvarsan is not absolutely free from the danger of causing optic neuritis, it is certainly less dangerous in this respect than atoxyl and arsacetin.

The toxic action of salvarsan on the *kidney* appears to be well marked. Albuminuria has been noted in many cases where it was absent before injection. Schlesinger and Gottheil have reported transient hæmaturia, with the passage of granular and hyaline casts. Werther and others have reported hæmorrhagic nephritis, and Mohr a case of hæmorrhagic nephritis with albuminuric retinitis. Cases of death

from anuria and uræmia have been recorded by Ravaut and Gaucher (*vide supra*).

The action of salvarsan on the *liver* is manifested by icterus, but this is rare. Milian only observed it six times in 1,500 cases. Hoffmann reported a fatal case in which acute yellow atrophy of the liver was found, but as this condition may be produced by syphilis itself, the case is not conclusive.

Deaths after Salvarsan. — The number of deaths which have occurred after injection of salvarsan is not known, for the reason that all cases have not been reported. Leredde has collected and analyzed fifty-four cases, but these only include adult cases reported by Continental observers, and do not include deaths in infants, nor cases reported in America and England. The total number of deaths is now probably not less than 100. How many of these were due to faulty technique or administration in unsuitable cases it is impossible to say, owing to the absence of detailed information in many instances; but it is certain that many deaths can be explained in this way. Leredde, in his analysis of 54 cases, divides them into 25 due to the action of salvarsan, 7 doubtful, and 22 independent of the drug; but he remarks that with few exceptions the deaths were due to faults of technique or non-observance of the contraindications. Many of the deaths in his analysis occurred in patients affected with advanced tabes, general paralysis, cerebral syphilis, and aortic disease. On the other hand, some of the cases which have been reported are difficult to explain, except by arsenical intoxication.

Contraindications. — Salvarsan appears to be contraindicated in advanced disease of the nervous system, heart and circulatory system, and kidneys. In myocarditis there is danger of fatal collapse if the injection is followed by a fall of blood-pressure. In disease of the coronary arteries the inflammatory reaction caused by the drug may occlude the vessel and cause death. In meningitis this reactionary inflammation may cause death by raising the intracranial pressure. In disease of the cranial vessels fatal hæmorrhage may occur after an injection. In chronic disease of the liver and kidneys fatal intoxication is liable to occur from deficient elimination

of the drug. Other contraindications are diabetes, advanced phthisis, old age, emaciation, and non-syphilitic affections of the eye.

Indications.—Salvarsan is said to be especially indicated in cases of malignant syphilis, in phagedena, in cases which resist the action of mercury, and in patients who cannot tolerate mercury. It is also recommended in ulcerative lesions, such as those of the pharynx, nose, and larynx, which are liable to result in cicatricial contraction during healing, the scar-tissue resulting after salvarsan being said to be softer and less in quantity than that resulting from the usual treatment. It is also recommended in the early stages of the chancre, with a view to abort the disease. Other indications differ according to different observers.

With regard to malignant syphilis, and cases resistant to mercury, it is remarkable what a number of such cases appear to have arisen since the introduction of salvarsan. As a matter of fact, malignant syphilis is rare, at any rate in Europe, and cases resistant to mercury still rarer. There are few cases which cannot be influenced by mercurial treatment when judiciously carried out, and combined with iodides and other accessory drugs.

In view of the conflicting opinions held as to the value of salvarsan, it is necessary to adopt a strictly impartial attitude, and sum up the evidence for and against. Thus, while some writers refer to it as an epoch-making discovery in therapeutics, and Wechselmann describes it as 'one of the most magnificent victories of civilization,' Gaucher regards it as an actual social danger, on account of the false security which it gives to patients, leading them to think themselves cured, neglect further treatment, and spread the disease when relapses occur; and Hallopeau considers that it should be abandoned, like atoxyl and arsacetin, on account of the numerous deaths which have been caused by it. While the former opinions undoubtedly err on the side of excessive enthusiasm, it is fair to state that Gaucher's objection will also apply to mercurial treatment, for it is only the minority of patients who carry out treatment for a sufficient length of time. However, consideri

the manner in which salvarsan has been brought before the notice of the public, Gaucher's warning is not untimely. Whether salvarsan will share the fate of atoxyl and arsacetin, or remain as an auxiliary form of treatment, remains to be seen. At any rate, although it produces remarkable effects in certain cases, it has not fulfilled all its original expectations, and is undoubtedly not free from danger, even when the strictest precautions are observed. In the meantime it is well to bear in mind that the great majority of cases of syphilis can be cured with mercury and iodides.

NOTE ON MERCURIAL TREATMENT.

The insoluble preparations of mercury used for injection (gray oil, calomel, and salicylate of mercury) are liable to form deposits at the site of injection, which may remain for a long time unabsorbed, but after some accidental trauma, may suddenly become absorbed and give rise to severe mercurial poisoning. Gaucher has collected ten cases of gangrenous stomatitis resulting from gray-oil injections, eight of which were fatal, and he mentions cases of fatal ulcerative colitis following injections of salicylate of mercury and calomel. For this reason I think it better to use soluble preparations for injection—especially the biniodide and benzoate, prepared according to Gaucher's formulæ. Both these are 1 per cent. solutions:

1. Benzoate of mercury ... ... 1 gramme.
   Chloride of sodium ... ... 2·5 grammes.
   Distilled water ... ... 100 c.c.
   Dose: 2 c.c. = 2 centigrammes = $\frac{1}{3}$ grain daily.

2. Biniodide of mercury } ... ... āā 1 gramme.
   Iodide of sodium }
   Distilled water ... ... 100 c.c.
   Dose = 2 c.c. = $\frac{1}{3}$ grain.

As regards pills, Hutchinson's pill of hydrarg. cum creta seems the best for average cases, although the 2-grain pil. hydrarg. is generally as good for the continuance of treatment after active symptoms have subsided. Of the other

pills, the protoiodide (gr. $\frac{1}{2}$) and the perchloride (gr. $\frac{1}{6}$) are useful in the early stages of syphilis, but these pills are not suitable for prolonged treatment.

At several recent discussions on the treatment of syphilis the so-called 'pill treatment' has been referred to in somewhat disparaging terms. The advocates of other methods say that it is the least efficacious of all methods, and some of them rely on the evidence of the Wassermann reaction to support their view. According to some observers, the 'pill treatment' has less effect than mercurial inunction or injections in transforming a positive Wassermann reaction into a negative one. Hence they argue that the 'pill treatment' is inferior to the other methods. In answer to this we have already seen (p. 514) that there is at present no evidence to show that the persistence of a positive Wassermann reaction has any prognostic or therapeutic significance. Further, the so-called 'pill treatment,' when properly carried out, includes all forms and combinations of internal administration of the various preparations of mercury and iodides, in conjunction with accessory drugs. A point to which sufficient attention is not usually given is that pills should be *uncoated*.

It has been stated that chronic glossitis is more common after 'pill treatment' than after other methods, and that this accounts for the greater frequency of cancer of the tongue in England. So far as I am aware, there is no evidence to support either of these statements. The incidence of glossitis is due, to a great extent, to absence of buccal hygiene, and as more care is given to this at Continental resorts such as Aix-la-Chapelle, this probably accounts for the comparative infrequency of glossitis.

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APPENDIX

METHODS OF STAINING THE SPIROCHÆTA PALLIDA.

Method of Giemsa.—This stain, which is recommended by Schaudinn, consists of a mixture of azure blue and eosine in methyl alcohol and glycerine (Romanowsky-Giemsa stain).

1. Fix the preparation in absolute alcohol for ten to fifteen minutes, or by exposing for a few seconds to osmic acid vapour.
2. Dilute the Giemsa solution with 10 volumes of distilled water, and stain for an hour.
3. Wash in distilled water, dry, and mount in balsam.

The *Spirochæta pallida* is stained pale rose, other spirochætes blue. Nuclei should be deep red if the preparation is sufficiently stained.

Method of Merino.—This is a modification of the above, and consists in the use of two solutions—an alcoholic solution of azure blue and a weak aqueous solution of eosin. It stains more rapidly (ten to fifteen minutes), but is less satisfactory than the method of Giemsa. The preparation, after fixing as above, is stained in the blue solution for a few minutes, and a few drops of the eosin solution are then added.

METHOD OF STAINING THE SPIROCHÆTA PALLIDA IN SECTIONS (Levaditi).

1. Fix small fragments of tissue in 10 per cent. formol for twenty-four hours.
2. Harden in alcohol, 96 per cent., for twenty-four hours.
3. Wash in distilled water for a few minutes till the fragments sink to the bottom of the vessel.
4. Soak in a solution of nitrate of silver, 3 per cent., for three to five days at a temperature of 38° C.
5. Wash in distilled water, and reduce in the following solution for twenty-four to forty-eight hours:

Pyrogallic acid, 2 to 4 per cent.
Formol, 5 c.c.
Distilled water, 100 c.c.

6. Wash in distilled water; dehydrate with alcohol; clear in xylol; imbed in paraffin, and cut sections.

7. Stain sections by one of the following methods:

(*a*) Giemsa's mixture for a few minutes; wash in water; fix in absolute alcohol containing a few drops of oil of cloves; clear with bergamot and xylol, and mount in Canada balsam.

(*b*) Concentrated solution of toluidine blue; fix in absolute alcohol with a few drops of glycerine-ether mixture; clear with bergamot and xylol, and mount in balsam.

By this method the spirochætes are stained black, the nuclei blue, and the connective and muscular tissues green.

[Leuriaux and Geets claim to have cultivated from syphilitic products 'a spirochæte which only arrives at this morphological state after having passed through a series of changes hitherto undescribed. It is derived from a globular or oval element which corresponds in form and dimensions to the *Cytorrhyctes luis* of Siegel, passes through a stage which resembles a trypanosome, and only attains the spirochæte form after a fresh series of changes.' They consider that 'the *Spirochæta pallida* is only one aspect of its protozoan life.'—*Centralblatt für Bakt.*, July 7, 1906. (*Vide* p. 37.)]

METHODS OF STAINING THE GONOCOCCUS.

1. For rapid diagnosis examination may be made on a slide, and the preparation examined without a cover-glass.

Smear a drop of pus on a glass slide; dry over a flame and stain for twenty seconds in a concentrated alcoholic solution of methylene blue; wash in water; dry, and examine with $\frac{1}{12}$ oil-immersion lens. The gonococci are stained blue, and are seen in pairs within the pus cells and sometimes free. The cocci are from 1 to 1·5 μ long and from 0·6 to 0·5 μ wide.

2. For permanent preparations stain in saturated alcoholic solution of eosin (warm) for three to five minutes; dry, and counterstain with saturated alcoholic solution of methylene blue for twenty seconds; wash in water, dry, and mount in balsam. The gonococci are stained blue; the protoplasm and eosinophile granules red.

3. *Gram's Method.*—The gonococcus is decolorized by Gram's method, which differentiates it from almost all other diplococci.

After staining as above (or for three to five minutes in aniline gentian violet), treat the stained film with the following solution till dark brown in colour:

Iodine	1 gramme.
Iodide of potassium	2 grammes.
Water	300 c.c.

Decolorize with absolute alcohol till the film appears almost colourless; dry, and mount in xylol balsam. The gonococci are decolorized, but other bacteria are blue; cellular tissues yellow; nuclei and mast cell granules blue.

CHIEF PREPARATIONS OF MERCURY USED FOR MERCURIAL INJECTIONS.

	Dose.	Percentage of Mercury.
SOLUBLE SALTS (for daily injections).		
Mercuric Iodide (Biniodide)	$\frac{1}{8}$ to $\frac{2}{3}$ grain	44
Alaninate (amido-propionate)	$\frac{1}{8}$ grain	53
Asparaginate (oxide of Hg + asparagine) ...	$\frac{1}{8}$ to $\frac{2}{3}$ grain	43
Benzoate	$\frac{1}{3}$ grain	45
Perchloride	$\frac{1}{8}$ grain	73
Cacodylate (oxide of Hg + cacodylic acid). [Only acts by biniodide, which it contains.] ...	$\frac{1}{8}$ grain	Variable
Cyanide	$\frac{1}{8}$ to $\frac{1}{4}$ grain	79
Hermophenyl (solution of oxide of Hg in phenol disulphonate of sodium)	$\frac{1}{3}$ grain	40
Lactate	$\frac{1}{8}$ to $\frac{1}{2}$ grain	52
Oxycyanide	$\frac{1}{4}$ grain	85
Salicylate (neutral)	$\frac{1}{3}$ grain	42
Sozoiodolate	$\frac{1}{4}$ grain	35
Succinimide	$\frac{1}{8}$ grain	50
INSOLUBLE SALTS (for weekly injections) [Suspended in sterilized oil of vaseline].		
Calomel	1 to 2 grains	84
Gray oil—		
Lang's formula:		
Mercury ... ... 2 parts		50
Sterilized anhydrous lanoline ... 1 part		
Sterilized liquid paraffin ... ... 1 ,,		
0·05 c.c. contains	4 centigrammes of Hg	
Lafay's formula:		
Mercury ... ... 40 parts		
Sterilized anhydrous lanoline ... 12 ,,		
Sterilized white vaseline ... .. 13 ,,		
Sterilized oil of vaseline ... ... 35 ,,		
Contains 50 centigrammes of Hg in 1 c.c.	6 to 12 centigrammes of Hg	40
Lambkin's formula:		
Mercury ... .1 ounce		
Anhydrous lanoline ... ...4 ounces		
Liquid paraffin (carbolized 2 per cent.) ... ... to 10 ,,	10 to 15 minims	10
Contains 1 grain of Hg in 10 minims		
Phenate	1½ grains	51
Protoiodide	2 grains	61
Salicylate (basic)	2 grains	59
Thymol acetate (acetate of Hg + alcoholic solution of thymol)	2 grains	56
Urate	2 grains	54

Levy-Bing, who has compared the action of the above preparations, comes to the conclusion that of the soluble preparations the *biniodide* is the best, and the lactate, neutral salicylate, benzoate, and hermophenyl also good. Of the insoluble preparations, *gray oil* is the best, and *calomel* should be reserved for severe cases requiring a heroic remedy.

CHIEF SUBSTANCES USED FOR INJECTION IN GONORRHŒA.

Bactericidal Agents:

Perchloride of mercury	1 in 10,000 to 1 in 4,000
Oxycyanide of mercury	1 in 4,000 to 1 in 2,000
Biniodide of mercury	1 in 4,000 to 1 in 2,000
Chloride of zinc	1 in 1,000 to 1 in 500
Permanganate of potassium	1 in 4,000 to 1 in 500
Permanganate of zinc	1 in 4,000 to 1 in 500
Liquor sodæ chlorinatæ	1 in 40
Ichthyol	1 in 100 to 5 in 100
Nitrate of silver	1 in 5,000 to 1,000 for injection; 1 to 5 per cent. for instillation
Protargol	1 in 400 to 1 in 100 for injection; 2 to 5 per cent. for instillation
Argonin	
Argentamin	
Largin	
Actol	1 to 10 per cent.
Itrol	
Ichthargan	1 in 5,000 to 1 in 500
Albargin	1 in 800 to 1 in 400

According to the experiments of Marshall and Neave, the new silver preparations are all powerful bactericides, with the exception of nargol, argyrol, and collargol, which have little or no bactericidal action. The percentage of silver is thus no criterion of the bactericidal power. The following are the percentages of silver found by these observers:

	Percentage of Ag.
Collargol	86·6
Silver fluoride	81·7
Silver nitrate	63·6
Itrol	60·8
Actol	51·5
Argentol	31·2
Ichthargan	27·1
Argyrol	20·0
Albargin	13·4
Nargol	9·6
Largin	9·4
Novargan	7·9
Protargol	7·4
Argentamine	6·4
Argonin	3·8

Astringent Agents:

Sulphate of zinc	1 in 200 to 1 in 100
Sulphocarbolate of zinc	1 in 200 to 1 in 100
Acetate of zinc	1 in 400 to 1 in 200
Sulphate of copper	1 in 400 to 1 in 200
Subacetate of lead	1 in 400 to 1 in 100
Alum	1 in 200 to 1 in 100
Tincture of perchloride of iron	1 in 100 to 2 in 100
Bismuth:	
Subnitrate of bismuth	grs. 8.
Mucilage of tragacanth, Glycerine	āā ℥ss.
Distilled water	to ℥i.
Mixed sulphates:	
Alum, Sulphate of zinc, Sulphate of iron, Sulphate of copper	āā gr. 1.
Distilled water	℥i.
Vegetable astringents:	
(1) Vini rubri	℥vi.
Acidi tannici	grs. xviii. (Ricord).
(2) Zinci sulphatis	grs. xv.
Plumbi acetatis	grs. xxx.
Tinct. catechu	℥i.
Vini opii	℥i.
Aquæ rosæ	℥vi. (Ricord).
(3) Zinci sulph.	grs. xv.
Plumbi acetat.	grs. xxx.
Ext. krameria	℥iii.
Tinct. opii	℥iii.
Aquæ	ad ℥vi. (Bumstead).
Ultzmann's injection:	
Carbolic acid, Sulphate of zinc, Alum	āā gr. ½.
Distilled water	℥i.
Motz's injection:	
Hermophenyl, Protargol	āā gr. ¼ to ½.
Glycerine	♏xv.
Cocaine	gr. ½.
Distilled water	℥i.

MERCURIAL PILLS.

1. Mercurial pill (blue mass)	grs. 2
Powdered opium	gr. ⅛.
2. Gray powder	grs. 1 to 2.
Comp. ipecac. powder	gr. ½ to 1.
3. Green iodide (protoiodide) of mercury	gr. ⅛ to 1.
Extract of gentian	gr. 1.
Extract of opium	gr. ⅛.

4. Fournier's modification of Ricord's pill :
   Protoiodide of mercury ... ... 5 centigrammes (gr. $\frac{1}{12}$).
   Extract of opium ... ... 1 centigramme (gr. $\frac{1}{60}$).

5. Fournier's modification of Dupuytren's pill :
   Perchloride of mercury ... } āā 1 centigramme (gr. $\frac{1}{60}$).
   Extract of opium ... ... }

6. Tannate of mercury ... ... grs. 2.
   Tannic acid ... ... gr. 1.

7. Plummer's pill :
   Calomel ... ... gr. 1.
   Sulphurated antimony ... ... gr. 1.
   Guaiacum resin ... ... grs. 2.
   Castor oil ... ... q.s.

8. Salicylate of mercury ... ... gr. $\frac{1}{3}$.

9. Mercurial pill ... ... gr. 1.
   Reduced iron ... ... grs. 2.
   Extract of gentian ... ... q.s.

MIXTURES.

1. Bicarbonate or citrate of potash ... grs. 15 to 20.
   Nitrate of potash ... ... grs. 3 to 5.
   Ether ... ... ♏v. to ♏x.
   Tincture of henbane ... ... ℥ss. to ℥i.
   Tartarated antimony ... ... gr. $\frac{1}{12}$ to $\frac{1}{8}$.
   Camphor water ... ... to ℥i.ss. (Berkeley Hill).

   Useful in acute gonorrhœa with chordee and in epididymitis.

2. Bicarbonate of potash ... ... grs. 5.
   Oil of yellow sandalwood ... ... ♏xv.
   Mucilage of tragacanth ... ... ℥i.
   Tincture of orange ... ... ♏xv.
   Water ... ... to ℥i.

   For declining stage of acute gonorrhœa.

3. Chlorate of potash ... ... grs. 15 to 20.
   Dilute hydrochloric acid ... ... ♏x.
   Spirit of chloroform ... ... ♏x.
   Infusion of cinchona ... ... ℥i.

   Useful in mercurial stomatitis.

4. Liquor hydrarg. perchlor. ... ... ℥ii.
   Iodide of potassium ... ... grs. 10.
   Compound tincture of cinchona ... ℥ss.
   Spirit of chloroform ... ... ♏x.
   Water ... . to ℥i.

   Useful in late secondary and relapsing syphilis.

OINTMENTS.

1. Unguentum cinereum (for mercurial inunction) :
   Mercury ... ... } āā ℥i.
   Lanoline ... ... }
   Olive oil ... ... ℥ss.

   Dose for inunction, ℥ss. to ℥i.

2. Calomel cream :

Calomel	... ...	℥i.
Lanoline	... ...	āā ℥ss.
Vaseline	... ...	

Useful for local treatment of secondary syphilides.

3. Unguentum iodi (1 per cent.) :

Iodine	... ...	grs. 5.
Iodide of potassium	... ...	grs. 20.
Glycerine	... ...	℥ii.
Vaseline	... ...	āā ℥ss.
Lanoline	... ...	

Useful in tertiary ulceration.

POWDERS.

1. Calomel ... ... 1 part.
   Oxide of zinc ... ... 2 parts.

Useful for condylomata.

2. Subacetate of copper ... ... 1 part.
   Powdered savin ... ... 3 parts.

Useful for small gonorrhœal warts.

3. Chlorate of potash ... ... } equal parts for
   Powdered cinchona .. ... } dentifrice.
   Prepared chalk ... ... }

ZITTMANN'S TREATMENT.

This is an empirical method of treatment for chronic rebellious cases of tertiary syphilis. The amount of mercury contained in the decoctions is infinitesimal, and the action is probably due to the combined effect of the ingestion of large quantities of fluid and diaphoresis.

The following directions are given by Sir Alfred Cooper :

The principle of the treatment consists in eliminating the poison from the system by sweating and purgation. The course of treatment lasts fourteen days. The patient is kept in a room the temperature of which is maintained at 80° F. The evening before commencing the treatment two of the following pills are administered :

℞ Hydrarg. subchlor. ... ... grs. ii.
Ext. col. co. ... ... grs. v.
Ext. hyoscyam. ... ... grs. ii.

M. ft. pil. ii.

The diet consists of, for breakfast, boiled egg or bacon, tea, no sugar or spices.

Lunch : butcher s meat, vegetables, no fruit.

Dinner : soup, fish, poultry.

For the first four days of the treatment the patient drinks ½ pint of the following decoction, as hot as possible, at 9 a.m., 10 a.m., 11 a.m., and 12 a.m. :

Decoction No. 1.

℞ Rad. sarzæ contus.		℥iv.
Sem. anisi contus.		āā ℥i. ℈i.
Sem. fœniculi contus.		
Fol. sennæ		℥i.
Rad. glycyrrh. contus.		℥iv.

Add in a linen bag:

Sacchar. alb.		āā ℥i. ℈i.
Alum. sulph.		
Hydr. subchlor.		℥i. ℈i.
Hydr. bisulph. rub.		℈i.
Aquæ		Cong. iii. (3 gallons).
	M.	

Boil gently down to 1 gallon, strain, and put into four 40-ounce bottles.

On the same days, at 3 p.m., 4 p.m., 5 p.m., and 6 p.m., the patient drinks ½ pint of the following decoction, No. 2, which is taken cold:

Decoction No. 2.

To the dregs from No. 1 decoction add:

Rad. sarzæ contus.		℥ii.
Cort. limon. contus.		āā ℥i.
Sem. cardam. contus.		
Rad. glycyrrh. contus.		
Aquæ		Cong. iii.

Boil gently down to 1 gallon, strain, and put into four 40-ounce bottles.

The patient is kept in bed except for one hour every evening, when he may sit up.

In the evening two pills are administered, the patient starting the decoctions again next day, as before. This treatment goes on in the same way until the fifteenth day, when it is discontinued.

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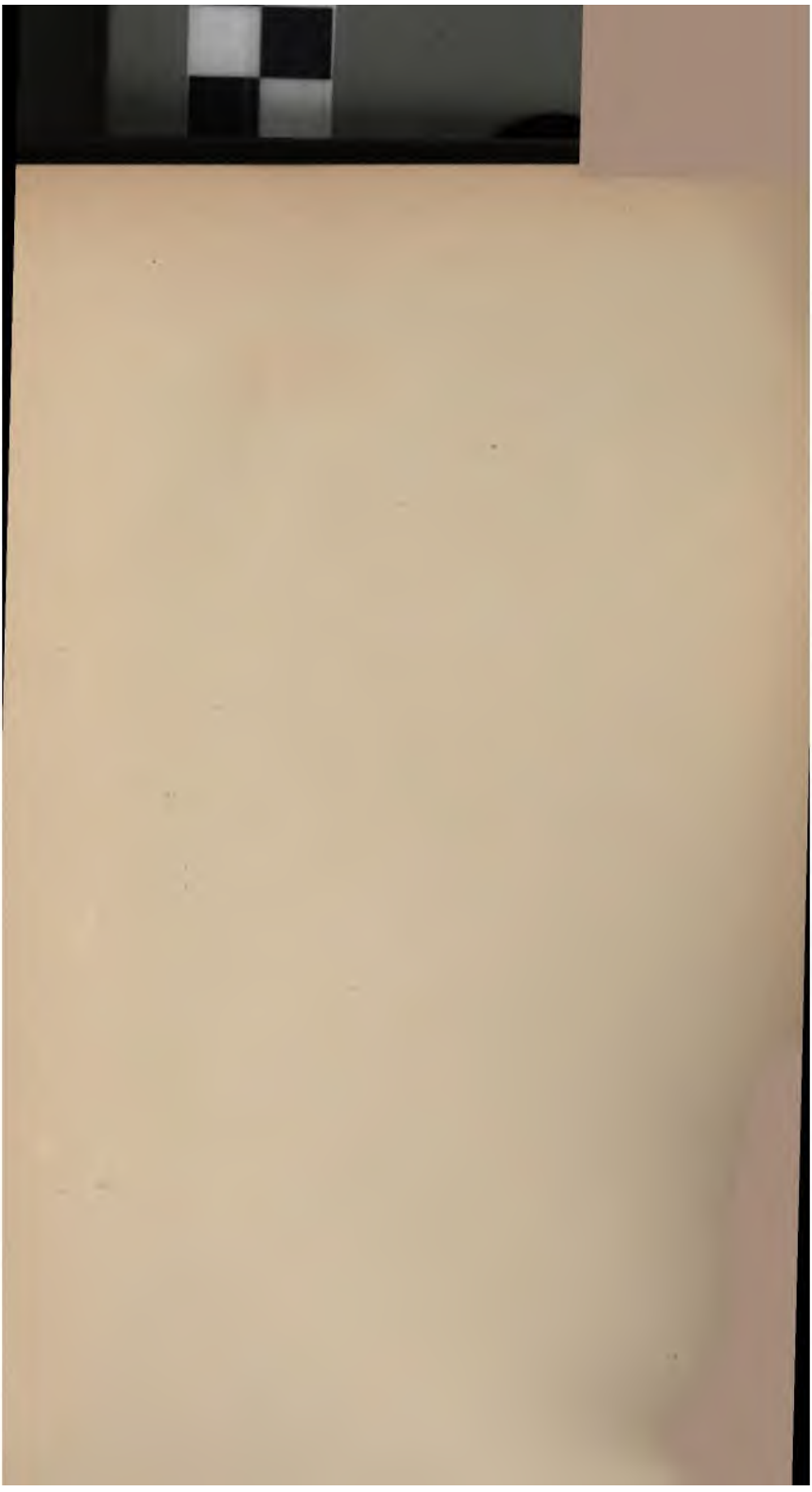

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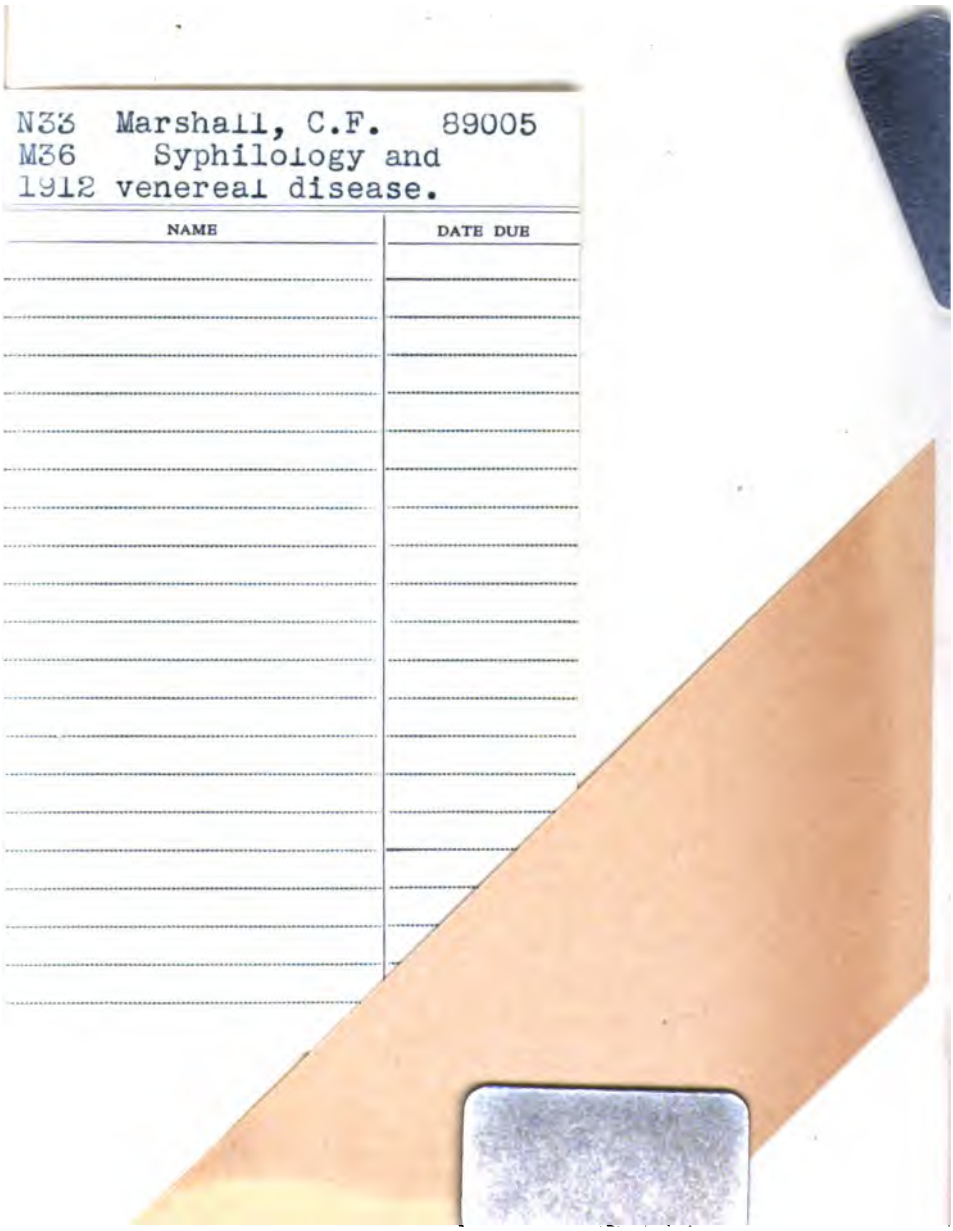

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